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FILE 'REGISTRY' ENTERED AT 07:30:27 ON 16 JUL 96

STRUCTURE FILE UPDATES: 12 JUL 96 HIGHEST RN 178357-08-9
DICTIONARY FILE UPDATES: 15 JUL 96 HIGHEST RN 178357-08-9

TSCA INFORMATION NOW CURRENT THROUGH DECEMBER 1995

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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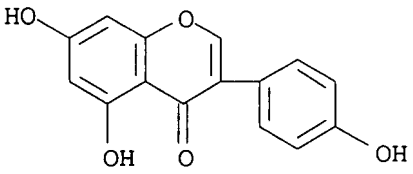
L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 1996 ACS
RN 446-72-0 REGISTRY
CN 4H-1-Benzopyran-4-one, 5,7-dihydroxy-3-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Genistein (6CI)**
CN Isoflavone, 4',5,7-trihydroxy- (8CI)
OTHER NAMES:
CN 4',5,7-Trihydroxyisoflavone
CN 5,7,4'-Trihydroxyisoflavone
CN C.I. 75610
CN Genisteol
CN Genisterin
CN Prunetol
CN Sophoricol
FS 3D CONCORD
MF C15 H10 O5
CI COM
LC STN Files: AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CAPREVIEWS, CASREACT, CEN, CHEMCATS, CHEMLIST, CIN, CJACS, CSCHEM, DDFU, DRUGU, EMBASE, HODOC*, IPA, MEDLINE, MRCK*, NAPRALERT, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



1 REFERENCES IN FILE CAPREVIEWS
828 REFERENCES IN FILE CA (1967 TO DATE)
15 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
831 REFERENCES IN FILE CAPLUS (1967 TO DATE)
34 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 125:32313

REFERENCE 2: 125:30713

REFERENCE 3: 125:30710

REFERENCE 4: 125:30085

REFERENCE 5: 125:30041

REFERENCE 6: 125:28922

REFERENCE 7: 125:25844

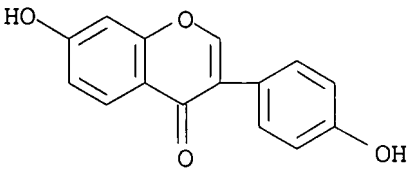
REFERENCE 8: 125:6235

REFERENCE 9: 125:5642

REFERENCE 10: 125:3434

=> d ide can l5

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 1996 ACS
RN 486-66-8 REGISTRY
CN 4H-1-Benzopyran-4-one, 7-hydroxy-3-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Daidzein (6CI)**
CN Isoflavone, 4',7-dihydroxy- (8CI)
OTHER NAMES:
CN 4',7-Dihydroxyisoflavone
CN 7,4'-Dihydroxyisoflavone
CN 7-Hydroxy-3-(4-hydroxyphenyl)-4H-1-benzopyran-4-one
CN Daidzeol
CN K 251b
FS 3D CONCORD
MF C15 H10 O4
CI COM
LC STN Files: ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CAPREVIEWS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CJACS, CSCHEM, DDFU, DRUGU, EMBASE, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



1 REFERENCES IN FILE CAPREVIEWS
542 REFERENCES IN FILE CA (1967 TO DATE)
9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
547 REFERENCES IN FILE CAPLUS (1967 TO DATE)
24 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 125:30085

REFERENCE 2: 125:5642

REFERENCE 3: 125:3434

REFERENCE 4: 124:352436

REFERENCE 5: 124:341722

REFERENCE 6: 124:341448

REFERENCE 7: 124:341447

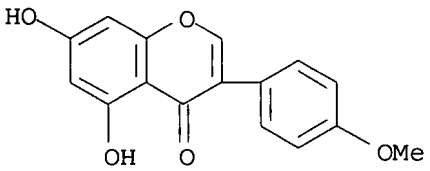
REFERENCE 8: 124:340921

REFERENCE 9: 124:337978

REFERENCE 10: 124:337447

=> d ide can 16

L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 1996 ACS
RN 491-80-5 REGISTRY
CN 4H-1-Benzopyran-4-one, 5,7-dihydroxy-3-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Biochanin A (6CI)
CN Isoflavone, 5,7-dihydroxy-4'-methoxy- (8CI)
OTHER NAMES:
CN 4'-Methylgenistein
CN 5,7-Dihydroxy-4'-methoxyisoflavone
CN **Biochanin**
CN Genistein 4-methyl ether
FS 3D CONCORD
MF C16 H12 O5
CI COM
LC STN Files: ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAOLD, CAPLUS, CAPREVIEWS, CASREACT, CHEMCATS, CHEMLIST, CJACS, CSCHEM, DDFU, DRUGU, EMBASE, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, SPECINFO, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



1 REFERENCES IN FILE CAPREVIEWS
333 REFERENCES IN FILE CA (1967 TO DATE)
333 REFERENCES IN FILE CAPLUS (1967 TO DATE)
26 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 125:28922

REFERENCE 2: 125:28594

REFERENCE 3: 124:337125

REFERENCE 4: 124:284064

REFERENCE 5: 124:241803

REFERENCE 6: 124:193572

REFERENCE 7: 124:115699

REFERENCE 8: 124:28798

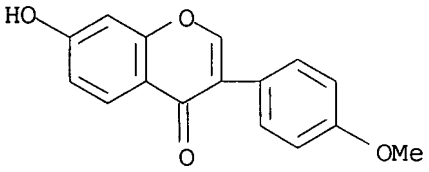
REFERENCE 9: 124:8440

REFERENCE 10: 123:306842

=> d ide can 17

L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 1996 ACS
RN 485-72-3 REGISTRY
CN 4H-1-Benzopyran-4-one, 7-hydroxy-3-(4-methoxyphenyl)- (9CI) (CA

INDEX NAME)
OTHER CA INDEX NAMES:
CN **Formononetin (6CI)**
CN Isoflavone, 7-hydroxy-4'-methoxy- (8CI)
OTHER NAMES:
CN 7-Hydroxy-4'-methoxyisoflavone
CN Biochanin B
CN Daidzein 4'-methyl ether
CN Formononetol
FS 3D CONCORD
MF C16 H12 O4
CI COM
LC STN Files: ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMLIST, CJACS, CSCHEM, DDFU, DRUGU, EMBASE, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, SPECINFO, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



467 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
468 REFERENCES IN FILE CAPLUS (1967 TO DATE)
38 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 125:5466

REFERENCE 2: 125:3434

REFERENCE 3: 124:352436

REFERENCE 4: 124:337125

REFERENCE 5: 124:284064

REFERENCE 6: 124:226906

REFERENCE 7: 124:226547

REFERENCE 8: 124:212205

REFERENCE 9: 124:185734

REFERENCE 10: 124:145739

=> d his l8-

(FILE 'REGISTRY' ENTERED AT 07:07:36 ON 16 JUL 96)
L8 27 S GENISTEIN?/CN
L9 17 S DAIDZEIN?/CN
L10 14 S BIOCHANIN?/CN
L11 11 S FORMONONETIN?/CN
L12 66 S L8 OR L9 OR L10 OR L11
L13 4 S L4 OR L5 OR L6 OR L7
L14 62 S L12 NOT L13

FILE 'HCAPLUS' ENTERED AT 07:09:17 ON 16 JUL 96
L15 1365 S L13 OR L13/D
E ESTROGEN/CT
L16 155 S E4-E8 (L) PHYTO/BI

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L17          64 S L15 AND L16
                E NUTRIENT/CT
L18           1 S E5 AND L17
L19        2077 S L4 OR L4/D OR GENISTEIN?/BI,AB OR L8 OR L8/D
L20         958 S L5 OR L5/D OR DAIDZEIN?/BI,AB OR L9 OR L9/D
L21         663 S L6 OR L6/D OR BIOCHANIN?/BI,AB OR L10 OR L10/D
L22         605 S L7 OR L7/D OR FORMONONETIN?/BI,AB OR L11 OR L11/D
L23           1 S (HEALTH (L) SUPPLEMENT#)/BI,AB AND (L19 OR L20 OR L21 O
L24       83285 S 57-88-5/BI,AB OR ?CHOLESTEROL?/IA
L25          28 S L24 AND (L19 OR L20 OR L21 OR L22)
L26       27563 S ((FOOD# OR FEED?)(L)(ADDITI? OR SUPPLEMENT?))/BI,AB
L27           4 S L26 AND (L19 OR L20 OR L21 OR L22)
                E DIET/CT
L28          14 S E3-E5 AND (L19 OR L20 OR L21 OR L22)
L29         114 S (NUTRITION OR NUTRIENT#)/SC,SX,BI,AB AND (L19 OR L20 OR
                E MENOPAUSE/CT
L30        2317 S E3
                E NEOPLAS/CT
L31      132726 S E4-E27
                E MAMMARY/CT
L32       21831 S E4-E8
                E OVAR/CT
L33       33527 S E4-E26
L34        2608 S L19 OR L20 OR L21 OR L22
L35           3 S L34 AND L30
L36         145 S L34 AND L31
L37          29 S L34 AND L32
L38          14 S L34 AND L33
                E FOOD/CT
L39       33649 S E3,E10
                E DIET
                E DIET/CT
L40       15529 S E3-E5
L41         170 S L35 OR L36 OR L37 OR L38
L42           1 S L41 AND L39
L43           5 S L41 AND L40
L44           6 S L42 OR L43
L45         140 S L34 AND (COMPN# OR COMPOSITION#)/BI,AB
L46          15 S L45 AND CLOVER/BI,AB
L47           1 S L46 AND 63/SC,SX
L48          13 S L45 AND PHARMACEUT?/SC,SX,BI,AB
L49          67 S L34 AND 63/SC
L50           9 S L41 AND L49
L51          25 S L18 OR L23 OR L27 OR L28 OR L42 OR L43 OR L47 OR L50

     FILE 'REGISTRY' ENTERED AT 07:30:27 ON 16 JUL 96

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 07:31:19 ON 16 JUL 96
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FILE COVERS 1967 - 16 Jul 1996  VOL 125 ISS 3
FILE LAST UPDATED: 17 Jul 1996  (960717/ED)

  A new table-of-contents alerting feature is available in the
  CAplus file.  Enter HELP TOC for details.

  Thesauri are now available for the WIPO International Patent
  Classifications (IPC) editions 1-6 in the /IC1, /IC2, /IC3, /IC4,
  /IC5, and /IC (/IC6) fields, respectively.  The thesauri in the
  /IC5 and /IC fields also include the corresponding catchword terms

=> d l51 1-25 cbib ab hitrn

L51  ANSWER 1 OF 25  HCAPLUS  COPYRIGHT 1996 ACS
1996:192494   Document No. 124:287925  A diet high in wheat fiber
     decreases the bioavailability of soybean isoflavones in a single
     meal fed to women.  Tew, Bee-Yen; Xu, Xia; Wang, Huei-Ju; Murphy,
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Patricia A.; Hendrich, Suzanne (Department Food Science Human Nutrition, Iowa State University, Ames, IA, 50011, USA). J. Nutr., 126(4), 871-7 (English) 1996. CODEN: JONUAI. ISSN: 0022-3166.

AB The absorption of some dietary components may be inhibited by dietary fiber. To study the effect of dietary fiber on the bioavailability of isoflavones, seven healthy women were randomly assigned in a crossover design to a control diet contg. 15 g dietary fiber or a wheat fiber-**supplemented** diet contg. 40 g dietary fiber, both fed with a single dose of 0.9 mg isoflavones/kg body wt. from tofu or texturized vegetable protein (TVP). The fiber-rich diet produced 55% lower plasma **genistein** at 24 h after soy dosing ($P < 0.03$). Urinary **daidzein** was not significantly related to fiber intake. Highly insol. dietary wheat fiber reduced the absorption of **genistein** probably by its bulking effect and hydrophobic binding to this compd. Urinary **genistein** was greater by 23% after tofu than after TVP consumption ($P < 0.02$), but the percentage of ingested **genistein** recovered in urine was not affected by soy product intake. The higher urinary **genistein** after tofu consumption compared with TVP was apparently due to differences in the amt. of **genistein**, not the different forms of **genistein** present in these two soy **food** products.

Date '96

IT **446-72-0**, **Genistein** **486-66-8**, **Daidzein**
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(a diet high in wheat fiber decreases the bioavailability of soybean isoflavones in a single meal fed to women)

L51 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 1996 ACS

1995:833184 Document No. 123:237794 Extraction of therapeutic genistin from soybean. Obata, Akio; Matsura, Masaru (Kikkoman Corp, Japan). Jpn. Kokai Tokkyo Koho JP 07173148 A2 950711 Heisei, 4 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 93-343304 931217.

AB A method for extn. and purifn. of therapeutic genistin from soybean involves: treating soybean isoflavon mixts. prepd. with the solvents $CHnCl_{4-n}$ [n = 0-2], concg. the exts., and subjecting to column chromatog. or TLC for purifn. The method was simple and time-saving.

IT **529-59-9P**, Genistin
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(extn. of therapeutic genistin from soybean)

L51 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 1996 ACS

1995:694807 Document No. 123:110724 Effect of diet on lignans and isoflavonoid phytoestrogens in chimpanzees. Musey, Paul I.; Adlercreutz, H.; Gould, K. G.; Collins, D. C.; Fotsis, T.; Bannwart, C.; Maekelae, T.; Waehaelae, K.; Brunow, G.; Hase, H. (Dep. Biol. Sci., Clark Atlanta Univ., Atlanta, GA, 30314, USA). Life Sci., 57(7), 655-64 (English) 1995. CODEN: LIFSAK. ISSN: 0024-3205.

Date is off. 95

AB Diphenolic compds. belonging to the classes of lignans and isoflavonoids have been identified in urine of man and animals, including the chimpanzee. Some of these compds., formed by intestinal bacteria from plant lignans and phytoestrogens, have been shown in animal studies to exhibit biol. activities that suggest they could function as cancer-protective compds. The effect of diet on urinary excretion of these compds. in the adult male chimpanzee has been studied. It was found that the chimpanzees consuming their regular food excreted large amts. of the isoflavonoid phytoestrogens, equol (mean .+-. SE) (127.5 .+-. 34.0 nmol/mg cr.) and **daidzein** (20.7 .+-. 9.0 nmol/mg cr.) and lignan, enterolactone (14.1 .+-. 3.5 nmol/mg cr.). Small amts. of the lignan, enterodiol, (0.4 .+-. 0.2 nmol/mg cr.) were also excreted. On all other four test diets (high protein, high carbohydrate, high vegetable, and high fat), the excretion was less, particularly on a high fat diet where the excretion of all diphenolic compds. was reduced by more than 90% to a level obsd. in omnivorous human subjects or women with breast cancer. These results suggest that

one component only

diet profoundly influences the excretion of both animal lignans and phytoestrogens urine. Because non-human primates are particularly resistant to mammary and genital carcinoma on estrogen treatment, the present data suggest that the very high levels of phytoestrogens and lignans was found during exposure to the regular diet may partially account for why these primates are so resistant to hormonal manipulations to induce cancer.

IT **486-66-8**, **Daidzein**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(diet effect on lignans and isoflavonoid phytoestrogens in chimpanzees)

L51 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 1996 ACS
1995:674220 Document No. 123:197595 Fecal lignan and isoflavonoid excretion in premenopausal women consuming flaxseed powder. Kurzer, Mindy S.; Lampe, Johanna W.; Martini, Margaret C.; Adlercreutz, Herman (Department of Food Science and Nutrition, University of Minnesota, St. Paul, MN, 55108, USA). Cancer Epidemiol., Biomarkers Prev., 4(4), 353-8 (English) 1995. CODEN: CEBPE4. ISSN: 1055-9965.
AB Lignans and isoflavonoids are diphenolic compds. found in plant **foods**, particularly whole grains and legumes. They have shown anticarcinogenic properties in animal and cell studies and have been assocd. with reduced cancer risk in epidemiol. studies. In order to perform further epidemiol. and metabolic studies on these compds., it is necessary to be able to monitor concns. in biol. samples. In this study, the effects of consumption of flaxseed, a concd. source of lignans, on fecal lignan excretion were examd. and the effect of high lignan consumption on fecal excretion of isoflavonoids was evaluated. Thirteen women were studied for 2 diet periods of 3 menstrual cycles each in a cross-over design. During the control period, they consumed their usual diets; during the treatment period they consumed their usual diets **supplemented** with 10 g/day ground flaxseed. Feces were collected on days 7-11 of the last menstrual cycle in each diet period. Five-day fecal composites were analyzed for lignans and isoflavonoids by isotope diln. gas chromatog.-mass spectrometry. Fecal excretion of the lignans enterodiol, enterolactone, and matairesinol increased significantly with flax consumption, from 80 to 2560, 640 to 10,300, and 7.33 to 11.9 nmol/day, resp. There were no differences in fecal excretion of the isoflavonoids **daidzein**, equol, **genistein**, and O-demethylangolensin.

Menopausal

L51 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 1996 ACS
1995:544100 Document No. 122:298750 Recent progress in the study of anticancer drugs originating from plants and traditional medicines in China. Han, Rui (Institute of Materia Medica, Chinese Academy of Medical Sciences, Beijing, 100050, Peop. Rep. China). Chin. Med. Sci. J., 9(1), 61-9 (English) 1994. CODEN: CMSJEP.
AB Drugs of plant origin have received much attention due to their enormous potential for the prevention and treatment of cancer. Recent progress in the study of anticancer drugs originating from plants and traditional medicines in China is reviewed with 28 refs., with particular emphasis on taxol, **daidzein**, acetyl boswellic acid, curcumin and ginsenoside Rh2.

only one

L51 ANSWER 6 OF 25 HCAPLUS COPYRIGHT 1996 ACS
1995:382260 Document No. 122:155682 Isotope dilution gas chromatographic-mass spectrometric method for the determination of unconjugated lignans and isoflavonoids in human feces, with preliminary results in omnivorous and vegetarian women. Adlercreutz, Herman; Fotsis, Theodore; Kurzer, Mindy S.; Waehaelae, Kristiina; Maekelae, Taru; Hase, Tapio (Dep. Clinicial Chem., Univ. Helsinki, Helsinki, FIN-00290, Finland). Anal. Biochem., 225(1), 101-8 (English) 1995. CODEN: ANBCA2. ISSN: 0003-2697.
AB The authors describe an isotope diln. gas chromatog.-mass spectrometric (GC/MS) method for the identification and quant. detn. of the lignans enterolactone, enterodiol, and matairesinol and the

isoflavonoids **daidzein**, equol, O-desmethylangolensin, and **genistein** in feces. Following the addn. of deuterated internal stds. for all compds., the feces samples are extd. and purified in several ion exchange chromatog. steps. Following formation of trimethylsilyl ethers, the samples are analyzed by combined capillary column GC/MS in the selective ion monitoring mode and cor. for all losses during the procedure using the deuterated internal stds. Results on the reliability of the method and values for nine Finnish omnivorous and nine vegetarian women are presented.

IT **446-72-0**, **Genistein 486-66-8**, **Daidzein**
RL: ANT (Analyte); ANST (Analytical study)
(isotope-diln. GC-MS detn. of unconjugated lignans and isoflavonoids in feces of omnivorous and vegetarian women)

L51 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 1996 ACS
1995:293259 Document No. 122:104521 Estrogen-specific 17.beta.-hydroxysteroid oxidoreductase type 1 (E.C. 1.1.1.62) as a possible target for the action of phytoestrogens. Maekelae, S.; Poutanen, M.; Lehtimaeki, J.; Kostian, M.-L.; Santti, R.; Vihko, R. (Institute Biomedicine, Univ. Turku, Turku, FIN-20520, Finland). Proc. Soc. Exp. Biol. Med., 208(1), 51-9 (English) 1995. CODEN: PSEBAA. ISSN: 0037-9727.

AB Several plant estrogens, esp. coumestrol and **genistein**, were found to reduce the conversion of [3H]estrone to [3H] 17.beta.-estradiol catalyzed by estrogen-specific 17.beta.-hydroxysteroid oxidoreductase Type 1 (E.C. 1.1.1.62) in vitro. Coumestrol, the most potent inhibitor in the expts., is the best inhibitor of the enzyme known to date. All compds. with inhibitory effects were also estrogenic. However, structural demands for 17.beta.-HSOR Type 1 inhibition and estrogenicity of tested compds. in breast cancer cells (judged by increased cell proliferation) were not identical. Zearalenone and diethylstilbestrol, both potent estrogens, did not inhibit 17.beta.-HSOR Type 1. Thus, changes in the estrogen mol. may discriminate between active sites of 17.beta.-HSOR Type 1 and estrogen binding sites of the ER. The effects of these compds. in vivo cannot be predicted on the basis of these results. Inhibition of 17.beta.-HSOR Type 1 enzyme could lead to a decrease in the availability of the highly active endogenous estrogen. However, these compds. are estrogenic per se, and they may thus replace endogenous estrogens. Addnl. studies are needed to further understand the role of these plant estrogens in the etiol. of hormone-dependent cancers. It is not easily conceivable how the chemopreventive action of Asian diets, possibly mediated by phytoestrogens in soya products, can be based on the inhibition of estrone redn. at the target cells by phytoestrogens or related compds., unless they are "incomplete estrogens" (i.e., unable to induce all effects typical of endogenous estrogens).

IT **446-72-0**, **Genistein 491-80-5**, **Biochanin A**
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); FFD (Food or feed use); BIOL (Biological study); PROC (Process); USES (Uses)
(estrogen-specific 17.beta.-hydroxysteroid oxidoreductase type 1 (E.C. 1.1.1.62) as possible target for action of phytoestrogens)

L51 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 1996 ACS
1994:708366 Document No. 121:308366 Method for treatment of menopausal and premenstrual symptoms. Gorbach, Sherwood L.; Goldin, Barry R.; Adlercreutz, Herman (Tufts University School of Medicine, USA). PCT Int. Appl. WO 9423716 A1 941027, 10 pp. DESIGNATED STATES: W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TT, UA, UZ, VN; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 94-US4189 940415. PRIORITY: US 93-49006 930416.

AB A method is provided for preventing or treating symptoms of

menopause, premenstrual syndrome, a condition resulting from reduced levels of endogenous estrogen, by administering to the woman an effective amt. of an isoflavonoid. The invention also features a therapeutic dietary product contg. isoflavonoids for preventing or treating symptoms of conditions resulting form reduced or altered levels of endogenous estrogen. The isoflavonoid is selected from the group consisting of **genistein**, **daidzein**, **biochanin** A, **formononetin**, O-desmethylangolensin, and equol.

IT **446-72-0**, **Genistein** **485-72-3**, **Formononetin** **486-66-8**, **Daidzein** **491-80-5**, **Biochanin** A
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(isoflavonoids for treatment of menopausal and premenstrual symptoms)

L51 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 1996 ACS
1994:693013 Document No. 121:293013 Dietary estrogens act through estrogen receptor-mediated processes and show no antiestrogenicity in cultured breast cancer cells. Makela, Sari; Davis, Vicki L.; Tally, William C.; Korkman, Johanna; Salo, Leena; Vihko, Reijo; Santti, Risto; Korach, Kenneth S. (Institute of Biomedicine, University of Turku, Turku, SF-20520, Finland). Environ. Health Perspect., 102(6-7), 572-8 (English) 1994. CODEN: EVHPAZ. ISSN: 0091-6765.

AB Dietary estrogens are believed to exert their estrogenic or antiestrogenic (chemopreventive) action in estrogen responsive cells by interacting with the estrogen receptor (ER). The present study was undertaken to evaluate a direct role of ER in estrogenic or antiestrogenic activities of three dietary estrogens (coumestrol, **genistein** and zearalenone). HeLa cells were transiently co-transfected with an expression vector for ER and an estrogen-responsive reporter gene construct. Coumestrol, **genistein**, and zearalenone all increased the activity of the reporter gene, only in the presence of the ER, and the activation was blocked with the ER antagonist ICI 164,384, demonstrating an ER-specific, agonist response. In addn., in MCF-7 cells, coumestrol and zearalenone increased the expression of the estrogen-responsive pS2 gene. Coumestrol and **genistein** inhibited the purified estrogen-specific 17.beta.-hydroxysteroid oxidoreductase enzyme and the conversion of estrone to 17.beta.-estradiol in T-47D cells, which contain this enzyme. However, they did not inhibit the estrone-induced proliferation of T-47D cells. In conclusion, coumestrol, **genistein**, and zearalenone are all potent estrogens in vitro, and they act through ER mediated mechanism. The authors findings give no evidence to support the idea that these compds. act as antiestrogens through competition for the binding sites of ER or by inhibition of the conversion of estrone to 17.beta.-estradiol in breast cancer cells, since this effect was nullified by their agonist action on cell proliferation. Therefore, their suggested chemopreventive action in estrogen-related cancers must be mediated through other mechanisms.

only one

IT **446-72-0**, **Genistein**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(dietary estrogens act through estrogen receptor-mediated processes and show no antiestrogenicity in cultured breast cancer cells)

IT **491-80-5**, **Biochanin** A
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(effect of dietary estrogens on estradiol formation in vitro)

L51 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 1996 ACS
1994:507102 Document No. 121:107102 soy intake and cancer risk: a review of the in vitro and in vivo data. Messina, Mark J.; Persky, Victoria; Setchell, Kenneth D. R.; Barnes, Stephen (Mt. Airy, MD, 21771, USA). Nutr. Cancer, 21(2), 113-31 (English) 1994. CODEN: NUCADQ. ISSN: 0163-5581.

AB A review with 112 refs. International variations in cancer rates have been attributed, at least in part, to differences in dietary intake. Recently, it has been suggested that consumption of soy foods may contribute to the relatively low rates of breast, colon, and prostate cancers in countries such as China and Japan. Soybeans contain a no. of anticarcinogens, and a recent National Cancer Institute workshop recommended that the role of soy foods in cancer prevention be investigated. In this review, the hypothesis that soy intake reduces cancer risk is considered by examg. relevant in vitro, animal, and epidemiol. data. Soybeans are a unique dietary source of the isoflavone **genistein**, which possesses weak estrogenic activity and has been shown to act in animal models as an antiestrogen. **Genistein** is also a specific inhibitor of protein tyrosine kinases; it also inhibits DNA topoisomerases and other crit. enzymes involved in signal transduction. In vitro, **genistein** suppresses the growth of a wide range of cancer cells, with IC50 values ranging from 5 to 40 .mu.M (1-10 .mu.g/mL). Of the 26 animal studies of exptl. carcinogenesis in which diets contg. soy or soybean isoflavones were employed, 17 (65%) reported protective effects. No studies reported soy intake increased tumor development. The epidemiol. data are also inconsistent, although consumption of nonfermented soy products, such as soymilk and tofu, tended to be either protective or not assocd. with cancer risk; however, no consistent pattern was evident with the fermented soy products, such as miso. Protective effects were obsd. for both hormone- and nonhormone-related cancers. While a definitive statement that soy reduces cancer risk cannot be made at this time, there is sufficient evidence of a protective effect to warrant continued investigation.

only one

L51 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 1996 ACS

1994:491781 Document No. 121:91781 Kudzu vine root extract, its preparation and use. Mai, Kai (Medical Science Institute of Henan Province, Peop. Rep. China). Faming Zhuanli Shenqing Gongkai Shuomingshu CN 1080287 A 940105, 8 pp. (Chinese). CODEN: CNXXEV. APPLICATION: CN 91-110602 911106.

AB The flavones I [R1, R2, R3 = H, H, H; H, glucopyranosyl, Me; H, glucopyranosyl, H; glucopyranosyl, H, H; H, glucopyranosyl, glucopyranosyl (4'7-diglycoside)] are extd. from Kudzu and tested for their antitumor activity. E.g., Kudzu (cut up in small pieces) was extd. twice with hot water, filtered, and concd. to 1/3-1/5 the original size; EtOH was added, the reaction mixt. was cooled to 10.degree. for 48-72 h, the EtOH was removed, water was added to ppt. the product at 0-10.degree., and the mixt. was filtered to give a liq. from which I (in powder form) was isolated. In an in vivo study using mice, this powder at 3 g/Kg effected 66.8% inhibition of stomach cancer.

IT **486-62-4 486-66-8 552-66-9 53681-67-7**
RL: BIOL (Biological study)
(antitumor, from Kudzu)

L51 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 1996 ACS

1994:105713 Document No. 120:105713 Chemopreventive phytochemicals in soy and licorice diets affecting key rat enzyme systems. Webb, T. E.; Stromberg, P. C.; Abou-Issa, H.; Moeschberger, M.; Pierson, H. F.; Curley, R. W., Jr. (Coll. Vet. Med., Ohio State Univ., Columbus, OH, 43210, USA). ACS Symp. Ser., 546(Food Phytochemicals for Cancer Prevention I), 361-71 (English) 1994. CODEN: ACSMC8. ISSN: 0097-6156.

AB As a component of a **feeding** study of the possible chemopreventive diet **additives** soybean meal and licorice root ext., simplified extn. and HPLC methods were developed for the anal. of the soy isoflavones **genistein** and **daidzein** and the licorice triterpenoids glycyrrhizic acid and glycyrrhetinic acid. In the diet contg. 25% soybean meal, **genistein** and **daidzein** were present at about 2-5 .mu.g/g of diet although some variability suggests these isoflavones, esp. **genistein**, may not be stable in frozen

diet exts. Markers glycyrrhizic and glycyrrhetinic acid showed the 3% licorice ext. contg. diet to be uniformly mixed and stable with final concns. of 300 and 20 .mu.g/g of diet each resp. Of these markers, only glycyrrhetinic acid was reliably detected in the plasma of rats fed the appropriate diet with an obsd. concn. of 5.83 .mu.g/mL.

IT **446-72-0, Genistein 486-66-8, Daidzein**
RL: BIOL (Biological study)
(of soybean meal, enzyme systems response to dietary)

L51 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 1996 ACS
1994:62290 Document No. 120:62290 **Health supplements** containing phytoestrogens, analogs, or metabolites thereof. Kelly, Graham Edmund (Australia). PCT Int. Appl. WO 9323069 A1 931125, 28 pp. DESIGNATED STATES: W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 93-AU230 930519. PRIORITY: AU 92-2511 920519.

AB **Compns**. enriched with natural phytoestrogens or analogs thereof selected from **genistein**, **daidzein**, **formononetin**, and **biochanin** A are used as **food additives**, tablets or capsules for promoting health in cases of cancer, premenstrual syndrome, menopause or hypercholesterolemia. Thus, dried red **clover** was extd. with a solvent mixt. contg. water, alc., $CHCl_3$, acetone, and/or EtOAc. Cholesterol-lowering effects of the obtained isoflavones were demonstrated with normal individuals.

IT **446-72-0, Genistein 485-72-3, Formononetin 486-66-8, Daidzein 491-80-5, Biochanin** A
RL: BIOL (Biological study)
(**health supplements** contg.)

L51 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 1996 ACS
1993:616833 Document No. 119:216833 Inhibition of tumor promoter-induced hydrogen peroxide formation in vitro and in vivo by **genistein**. Wei, Huachen; Wei, Lihong; Frenkel, Krystyna; Bowen, Ronald; Barnes, Stephen (Dep. Environ. Health Sci., Univ. Alabama, Birmingham, AL, 35294, USA). Nutr. Cancer, 20(1), 1-12 (English) 1993. CODEN: NUCADQ. ISSN: 0163-5581.

AB Here the authors report that **genistein**, a soybean isoflavone, strongly inhibits tumor promoter-induced H_2O_2 formation both in vivo and in vitro. **Genistein** suppressed H.infin.O_2 prodn. by 12-O-tetradecanoylphorbol-13-acetate- (TPA) stimulated human polymorphonuclear leukocytes (MNs) and HL-60 cells in a dose-dependent manner over the concn. range 1-150 .mu.M. Human PMNs were more sensitive to the inhibitory effect of **genistein** than HL-60 cells (50% inhibitory concn. 14.8 and 30.2 .mu.M, resp.). In addn., **genistein** moderately inhibited superoxide anion formation by HL-60 cells and scavenged exogenously added H_2O_2 under the same conditions as in cell culture. However, the H_2O_2-scavenging effect of **genistein** was about 50% lower than its inhibition of cell-derived H_2O_2 formation at all concns. In the CD-1 mouse skin model, **genistein** strongly inhibited TPA-induced oxidant formation, edema, and PMN infiltration in mouse skin. Inhibition of TPA-mediated H_2O_2 in vivo may result from decreased cell-derived H_2O_2 formation, scavenging of H_2O_2 produced, and/or suppression of PMN infiltration into the dermis. The antioxidant properties of **genistein** may be responsible for its anticarcinogenic effects, and the dietary availability of **genistein** makes it a promising candidate for the prevention of human cancers.

IT **446-72-0, Genistein**
RL: BIOL (Biological study)
(inhibition of tumor promoter-induced hydrogen peroxide formation by)

L51 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 1996 ACS
1993:558753 Document No. 119:158753 Nutritive quality of the alkaloid-poor Washington lupine (Lupinus polyphyllus Lindl var SF/TA) as a potential protein crop. Aniszewski, Tadeusz (Dep. Biol., Univ. Joensuu, Joensuu, 80101, Finland). J. Sci. Food Agric., 61(4), 409-21 (English) 1993. CODEN: JSFAAE. ISSN: 0022-5142.
AB An alkaloid-poor line of Washington lupine (L. polyphyllus var SF/TA) was developed in an expt. started in 1982. The nutritive quality (alkaloid content, protein and amino acids, fat and fatty acids, macro- and micronutrients, fiber, sugars) yields, and seed quality of this line were studied. The total alkaloid content was low and varied in different seeds from 226 to 366 .mu.g/g of dry matter. The main alkaloid was lupanine, but 16 other alkaloids (including sparteine and gramine) were also present. The var SF/TA cannot yet be used for human nutrition without processing although it would be a valuable protein crop. The results confirm that seeds which look different also vary in chem. compn.
IT **446-95-7**, .alpha.-Isosparteine
RL: BIOL (Biological study)
(of alkaloid-poor Washington lupine)

L51 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 1996 ACS
1993:225302 Document No. 118:225302 **Genistein**, a dietary-derived inhibitor of in vitro angiogenesis. Fotsis, Theodore; Pepper, Michael; Adlercreutz, Herman; Fleischmann, Gudrun; Hase, Tapio; Montesano, Roberto; Schweigerer, Lothar (Child. Hosp., Ruprecht-Karls-Univ., Heidelberg, 6900, Germany). Proc. Natl. Acad. Sci. U. S. A., 90(7), 2690-4 (English) 1993. CODEN: PNASA6. ISSN: 0027-8424.
AB Consumption of a plant-based diet can prevent the development and progression of chronic diseases that are assocd. with extensive neovascularization; however, little is known about the mechanisms. To det. whether prevention might be assocd. with dietary-derived angiogenesis inhibitors, the authors have fractionated urine of healthy human subjects consuming a plant-based diet and examd. the fractions for their abilities to inhibit the proliferation of vascular endothelial cells. Using gas chromatog.-mass spectrometry, the authors showed that one of the most potent fractions contained several isoflavonoids, which were subsequently synthesized. Of all synthetic compds., the isoflavonoid **genistein** was the most potent and inhibited endothelial cell proliferation and in vitro angiogenesis at concns. giving half-maximal inhibition of 5 and 150 .mu.M, resp. **Genistein** concns. in urine of subjects consuming a plant-based diet are in the micromolar range, while those of subjects consuming a traditional Western diet are lower by a factor of >30. The high excretion of **genistein** in urine of vegetarians and the present results suggest that **genistein** may contribute to the preventive effect of a plant-based diet on chronic diseases, including solid tumors, by inhibiting neovascularization. Thus, **genistein** may represent a member of a new class of dietary-derived anti-angiogenic compds.
IT **446-72-0**, **Genistein**
RL: BIOL (Biological study)
(vascular endothelial cell proliferation and angiogenesis inhibition by, of urine of humans consuming plant-based diet)
IT **486-66-8**, **Daidzein**
RL: BIOL (Biological study)
(vascular endothelial cell proliferation inhibition by, of urine of humans consuming plant-based diet)

L51 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 1996 ACS
1992:401168 Document No. 117:1168 Dietary phytoestrogens and cancer: in vitro and in vivo studies. Adlercreutz, Herman; Mousavi, Yaghoob; Clark, Jim; Hockerstedt, Krister; Hamalainen, Esa; Wahala, Kristiina; Makela, Taru; Hase, Tapio (Dep. Clin. Chem., Univ. Helsinki, Helsinki, SF-00290, Finland). J. Steroid Biochem. Mol.

Biol., 41(3-8), 331-7 (English) 1992. CODEN: JSBBEZ. ISSN: 0960-0760.

AB Postmenopausal women (11 omnivores, 10 vegetarians, and 9 apparently healthy women with surgically removed breast cancer) were investigated with regard to the assocn. of their urinary excretion of estrogens, lignans, and isoflavonoids (all diphenols) with plasma sex hormone binding globulin (SHBG). A pos. correlation between urinary total diphenol excretion and plasma SHBG was found which remained significant after elimination of the confounding effect of body mass detd. by body mass index (BMI). Furthermore there was a neg. correlation between plasma SHBG and urinary excretion of 16.alpha.-hydroxyestrone and estriol which also remained significant after eliminating the effect of BMI. Enterolactone (Enl) stimulates the synthesis of SHBG by HepG2 liver cancer cells in culture acting synergistically with estradiol and at physiol. concns. Enl was rapidly conjugated by the liver cells, mainly to its monosulfate. Several lignans and the isoflavonoids **daidzein** and equol compete with estradiol for binding to the rat uterine type II estrogen binding site (the s.c. bioflavonoid receptor). It is suggested that lignans and isoflavonoids may affect uptake and metab. of sex hormones by participating in the regulation of plasma SHBG levels an in this way influence their biol. activity and that they may inhibit cancer cell growth like some flavonoids by competing with estradiol for the type II estrogen binding sites.

one component

IT **486-66-8**, **Daidzein**
RL: PROC (Process)
(binding of, by estrogen receptors of uterus, mammary tumor in women in relation to)

L51 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 1996 ACS

1992:221608 Document No. 116:221608 Neoplasm inhibitors containing flavonoids and C18-22 .omega.-3 type higher unsaturated fatty acid-contg. phosphatidylcholines and their preparations. Hibino, Hidehiko; Fukuda, Nobuo; Asahi, Kenichi; Sakurai, Shigeru; Takahashi, Nobutaka (Nippon Oil and Fats Co., Ltd., Japan; Institute of Physical and Chemical Research). Jpn. Kokai Tokkyo Koho JP 03275625 A2 911206 Heisei, 9 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 90-72163 900323.

AB The neoplasm inhibitors are prepd. by (i) emulsifying the mixt. of flavonoids and phosphatidylcholines by 0.01-5 wt.% polyoxyethylene hydrogenated castor oil as a surfactant, or (ii) dissolving the mixt. in a single or multiple solvents, evapg., and then emulsifying. Sn-1-oleoyl-Sn-2-docosahexaenoyl-phosphatidylcholine (1500 mg) and 225 mg apigenin were dissolved into 10 mL pyridine and freeze-dried, which were vibration-stirred with H2O to 150 mL to give a suspension. The suspension given to tumor-bearing mice at 0.4 mL i.p. 7 times for 14 days showed 44.7 av. survival days vs. 40.7 days for the untreated controls.

IT **446-72-0**, **Genistein**
RL: BIOL (Biological study)
(neoplasm inhibitors contg. C18-22 .omega.-3 type higher unsatd. fatty acid-contg. phosphatidylcholines and)

L51 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 1996 ACS

1992:58033 Document No. 116:58033 Urinary excretion of lignans and isoflavonoid phytoestrogens in Japanese men and women consuming a traditional Japanese diet. Adlercreutz, Herman; Honjo, Hideo; Higashi, Akane; Fotsis, Theodore; Hamalainen, Esa; Hasegawa, Takeshi; Okada, Hiroji (Dep. Clin. Chem., Univ. Helsinki, Helsinki, USF-00290, Finland). Am. J. Clin. Nutr., 54(6), 1093-100 (English) 1991. CODEN: AJCNAC. ISSN: 0002-9165.

AB Epidemiol. studies revealed low mortality in hormone-dependent cancer in Japanese women and men consuming a traditional diet. It was previously found that certain diphenolic food components, lignans and isoflavonoids, which are converted to biol. active hormone-like substances by intestinal microflora, may be cancer-protecting agents. Therefore, urinary excretion of these compds. (enterolactone, enterodiol, **daidzein**, equol, and O-desmethylangolensin) was studied in 10 women and 9 men in a rural

village south of Kyoto, Japan. The subjects consumed a typical low-fat diet with much rice and soy products, fish, and vegetables. An isotope-diln. gas chromatog.-mass spectrometric method was used for the assays. The urinary excretion of lignans was low but that of the isoflavonoids was very high. The excretion of isoflavonoids correlated with soybean-product intake. The low mortality in breast and prostate cancer of Japanese women and men, resp., may be due to the high intake of soybean products.

IT **486-66-8**
RL: BIOL (Biological study)
(of food plants, in urine of humans consuming traditional Japanese diet, breast and prostate cancer in relation to)

L51 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 1996 ACS
1990:104847 Document No. 112:104847 Isolation of isoflavone aglycones (as anticancer agents) from soybeans. Obata, Akio; Matsura, Masaru; Hashimoto, Hikotaka (Kikkoman Corp., Japan). Jpn. Kokai Tokkyo Koho JP 01258669 A2 891016 Heisei, 4 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 88-83185 880406.

AB The title compds. are extd. by heating (ground) soybeans at 45-55.degree. to maximize .beta.-glucosidase activity in soybeans. The isoflavones [**daidzein** and **genistein**] as aglycon are useful as anticancer agents (no data). Skinned soybeans (5 kg) in 25 L H2O were ground at 50.degree., kept at 50.degree. for 1 h, lyophilized, powd., defatted via Soxhlet extn. with hexane, and extd. with ether to give 7.2 g isoflavone aglycons.

IT **446-72-0**, **Genistein 486-66-8**, **Daidzein**
RL: PROC (Process)
(isolation of, as anticancer agent from soybeans)

L51 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 1996 ACS
1987:175077 Document No. 106:175077 Determination of urinary lignans and phytoestrogen metabolites, potential antiestrogens and anticarcinogens, in urine of women on various habitual diets. Adlercreutz, H.; Fotsis, T.; Bannwart, C.; Wahala, K.; Makela, T.; Brunow, G.; Hase, T. (Meilahti Hosp., Univ. Helsinki, Helsinki, SF-00290, Finland). J. Steroid Biochem., 25(5B), 791-7 (English) 1986. CODEN: JSTBBK. ISSN: 0022-4731.

AB Five compds., the lignans enterolactone [78473-71-9] and enterodiol [80226-00-2], and the isoflavonic phytoestrogen metabolites **daidzein** [**486-66-8**], equol [531-95-3], and O-desmethylangolensin [21255-69-6], were measured by GC-MS in the urine of 5 groups of women (total no. 53). The members of 3 dietary groups (omnivores, lactovegetarians, and macrobiotics) were living in Boston and 2 groups in Helsinki (omnivores and lactovegetarians). Measurements were carried out in 94 72-h samples. The highest mean excretion of the most abundant compd., enterolactone, was found in the macrobiotic group and the lowest by the omnivores. Total mean 24-h excretion of enterolactone was 17,680 nmol in the macrobiotics, 4170 nmol in the Boston lactovegetarians, 3650 nmol in the Helsinki lactovegetarians, 2460 nmol in the Helsinki omnivores, and 2050 nmol in the Boston omnivores. The other diphenols followed approx. the same pattern. In an earlier study, the lowest excretion of enterolactone (1040 nmol/24 h) was found in a group of postmenopausal apparently healthy breast cancer patients living in Boston. It is concluded that further studies are necessary to elucidate the possible role of these compds. in cancer and other diseases. However, the evidence obtained seems to justify the conclusion that these compds. may be among the dietary factors affording protection against hormone-dependent cancers in vegetarians and semivegetarians.

only one

IT **486-66-8**, **Daidzein**
RL: BIOL (Biological study)
(of urine, of women, diet compn. effect on)

L51 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 1996 ACS
1986:95475 Document No. 104:95475 Antitumor pharmaceuticals. Takahashi, Nobutaka; Asahi, Kenichi; Takuma, Tomoko; Mikawa, Ushio;

Kinoshita, Takeshi (Institute of Physical and Chemical Research, Japan). Jpn. Kokai Tokkyo Koho JP 60178815 A2 850912 Showa, 8 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 84-33756 840224.

AB Antitumor pharmaceuticals for oral or parenteral administration contain compds. selected from dimethylmelannein and derivs. of chalcone, dihydrochalcone, flavanone, isoflavanone, roteinoid, isoflavan, isoflavene, pterocarpan, coumestan and 3-arylcoumarin. Thus, 10 mg liquiritigenin and 5 g glucose were mixed and filled with vials to produce an injection prepn. The prepn. was dissolved in EtOH and mixed with 0.85% saline (100 mL) prior to i.v. administration. In vitro antineoplastic activities of these compds. were demonstrated with mouse erythroid leukemia cells, mouse myeloid leukemia cells, and mouse tetracarcinoma cells.

IT **552-66-9**
RL: BIOL (Biological study)
(antitumor pharmaceuticals contg.)

L51 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 1996 ACS

1984:443586 Document No. 101:43586 Antitumor formulations containing flavonoids. (Institute of Physical and Chemical Research, Japan). Jpn. Kokai Tokkyo Koho JP 59046217 A2 840315 Showa, 8 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 82-157103 820909.

AB Antitumor formulations contain flavonoids or isoflavonoids (I and II), where R1, R2, R3, and R4 = H, OH, or OMe; R5 and R6 = H, OH, OMe, or 3,4,5-R7R8R9C6H2 (R7, R8, and R9 = H, OH, or OMe). Thus, 10 mg **genistein** (I, R1 = R3 = OH, R2 = R4 = R5 = H, R6 = 4-HOC6H4) [**446-72-0**] was mixed with 5 g glucose powder and sealed in a vial with an inert gas. Immediately before its use, the mixt. was dissolved in EtOH and combined with 100 mL 0.85% saline to give an i.v. injection soln. The antitumor activity against mouse erythroid leukemia cells was demonstrated in vitro.

IT **446-72-0 486-66-8**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor formulations contg.)

L51 ANSWER 24 OF 25 HCAPLUS COPYRIGHT 1996 ACS

1984:115110 Document No. 100:115110 Identification of the isoflavonic phytoestrogen **daidzein** in human urine. Bannwart, Christoph; Fotsis, Theodore; Heikkinen, Risto; Adlercreutz, Herman (Dep. Clin. Chem., Univ. Helsinki, Helsinki, Finland). Clin. Chim. Acta, 136(2-3), 165-72 (English) 1984. CODEN: CCATAR. ISSN: 0009-8981.

AB The identification by gas chromatog.-mass spectrometry of the isoflavonic phytoestrogen **daidzein** [7-hydroxy-3-(4-hydroxyphenyl)-4H-1-benzopyran-4-one](I) [**486-66-8**] for the first time in human urine is described. The metab. and effect on reprodn. of isoflavones in animals and the possible significance of phytoestrogens in man is discussed. Preliminary results on the quant. excretion of **daidzein** in female subjects consuming different diets are also reported.

IT **486-66-8**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in urine of human)

L51 ANSWER 25 OF 25 HCAPLUS COPYRIGHT 1996 ACS

1980:562443 Document No. 93:162443 Occurrence, formation, and precursors of N-nitroso compounds in Japanese diet. Kawabata, Toshiharu; Ohshima, Hiroshi; Uibu, Jaak; Nakamura, Masamichi; Matsui, Masami; Hamano, Miyoko (Dep. Biomed. Res. Foods, NIH, Tokyo, Japan). Proc. Int. Symp. Princess Takamatsu Cancer Res. Fund, 9th(Nat. Occurring Carcinog.-Mutagens Modulators Carcinog.), 195-209 (English) 1979. CODEN: PPTCBY.

AB Data on the nitrosamine content of various fermented foods indicate that a range from almost no detectable level to trace quantities of nitrosamines nitrosodimethylamine [62-75-9], and nitrosopyrrolidine [930-55-2] could be detected in various fermented sauce, vinegar, miso, sake, beer, etc. The nitrosamine content of salt-dried fish and shellfish increased when these products were broiled in a gas range. This was very conspicuous in the case of dried squid, with

the highest instance being 313 .mu.g/kg. Covering dried fish with Al foil or broiling in an elec. range was highly effective in decreasing the degree of nitrosamine formation. No alkylureas were detected in salt-dried fish products, including the original uncooked products and those broiled in a gas range. Green tea exts. enhanced the nitrosation of secondary amines Me2NH [124-40-3], Et2NH [109-89-7], pyrrolidine [123-75-1], piperidine [110-89-4] at specific pH (3.0 or 3.4) and tea ext. concn. Among various polyphenols in green tea, only catechins catalyzed nitrosamine formation, whereas pyrocatechol [120-80-9], pyrogallol [87-66-1], and gallic acid [149-91-7] inhibited the reaction. Flavonols or flavones in tea had no effect on the nitrosation reaction.

IT **446-72-0**
RL: BIOL (Biological study)
(of green tea ext., nitrosamine formation and carcinogenicity in relation to)

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(FILE 'REGISTRY' ENTERED AT 07:30:27 ON 16 JUL 96)

FILE 'HCAPLUS' ENTERED AT 07:31:19 ON 16 JUL 96

FILE 'MEDLINE' ENTERED AT 07:32:02 ON 16 JUL 96

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L52          699 S L4
L53          699 S GENISTEIN/CN,CT
L54           78 S L5
L55           78 S DAIDZEIN/CN,CT
L56           18 S L6
L57           18 S BIOCHANIN A/CN,CT
L58           14 S L7
L59           14 S FORMONONETIN/CN,CT
L60          743 S L52 OR L53 OR L54 OR L55 OR L56 OR L57 OR L58 OR L59
L61          138 S L60 AND C4./CT
L62         1011 S ISOFLAVONES+NT/CT
L63           61 S L62/MAJ AND L61
L64           17 S L60 AND DIET+NT/CT
L65           54 S L60 AND J1./CT
L66           17 S L60 AND NUTRITION+NT/CT
L67            0 S L60 AND FOOD ADDITIVES+NT/CT
L68           59 S L64 OR L65 OR L66
L69           13 S L68 AND C4./CT
L70            1 S L68 AND MENOPAUSE+NT/CT
L71            3 S C19.146./CT AND L68
L72            1 S L68 AND CHOLESTEROL+NT/CT
L73            0 S L68 AND C18./CT
L74           14 S L69 OR L70 OR L71 OR L72
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FILE 'EMBASE' ENTERED AT 07:45:49 ON 16 JUL 96

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L75         1090 S L4
L76         1154 S GENISTEIN/CT
L77          145 S L5
L78          184 S DAIDZEIN/CT
L79           62 S L6
L80           68 S BIOCHANIN A/CT
L81           35 S L7
L82           79 S FORMONONETIN/CT
L83         1256 S L75 OR L76 OR L77 OR L78 OR L79 OR L80 OR L81 OR L82
L84          152 S L83 AND NUTRITION+NT/CT
L85            6 S L83 AND DIET SUPPLEMENTATION/CT
L86           36 S L83 AND INDUSTRIAL CHEMICAL+NT/CT
L87            1 S L86 AND FOOD ADDITIVE/CT
L88            0 S L83 AND ("MENOPAUSE AND CLIMACTERIUM"+NT)/CT
L89            1 S L83 AND MENSTRUATION DISORDER+NT/CT
L90            8 S L83 AND MENSTRUAL CYCLE+NT/CT
L91          285 S L83 AND C6.610./CT
L92          253 S L77 OR L78 OR L79 OR L80 OR L81 OR L82
L93           61 S L92 AND L91
L94           28 S L93 AND L84
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L95         1155 S L75 OR L76
L96          125 S L95 AND L84
L97           15 S DIET/CT AND L96
L98          532 S ((GENISTEIN OR DAIDZEIN OR BIOCHANIN A OR FORMONONETIN)
L99           55 S L98 AND L84
L100          75 S L85 OR L87 OR L89 OR L90 OR L97 OR L99
L101           9 S L94 NOT L100
L102          84 S L100 OR L94

     FILE 'MEDLINE, EMBASE' ENTERED AT 08:04:52 ON 16 JUL 96
L103          94 DUP REM L74 L102 (4 DUPLICATES REMOVED)

     FILE 'EMBASE' ENTERED AT 08:05:33 ON 16 JUL 96

     FILE 'MEDLINE' ENTERED AT 08:05:44 ON 16 JUL 96
L104           2 FILE EMBASE
L105          12 S L74 NOT L104

     FILE 'EMBASE' ENTERED AT 08:06:36 ON 16 JUL 96
L106          13 S L102 NOT AB/FA
L107          71 S L102 NOT L106

     FILE 'MEDLINE, EMBASE' ENTERED AT 08:06:55 ON 16 JUL 96
L108          15 DUP REM L104 L106 (0 DUPLICATES REMOVED)
L109          79 DUP REM L105 L107 (4 DUPLICATES REMOVED)

=> fil medline embase
FILE 'MEDLINE' ENTERED AT 08:07:20 ON 16 JUL 96

FILE 'EMBASE' ENTERED AT 08:07:20 ON 16 JUL 96
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=> d l108 1-15 cbib ab ct

L108 ANSWER 1 OF 15  EMBASE  COPYRIGHT 1996 ELSEVIER SCI. B.V.
95358157  EMBASE  Suppression by anticancer agents of reactive oxygen
     generation from polymorphonuclear leukocytes. Ueta E.; Osaki T..
     Department of Oral Surgery, Kochi Medical School, Oko-cho,
     Nankoku-city, Kochi 783, Japan. Free Radical Research  24/1 (39-53)
     1996. ISSN: 1071-5762. CODEN: FRARER. Pub. Country: United Kingdom.
     Language: English. Summary Language: English.
CT   EMTAGS: blood and hemopoietic system (0927); chemical procedures
     (0107); mammal (0738); human (0888); controlled study (0197); human
     tissue, cells or cell components (0111); article (0060);
     radioisotope (0131); enzyme (0990)
     Medical Descriptors:
     *neutrophil
     *respiratory burst
     drug mechanism
     calcium cell level
     enzyme activity
     protein phosphorylation
     radiation
     chemoluminescence
     signal transduction
     human
     controlled study
     human cell
     article
     Drug Descriptors:
     *antineoplastic agent: PD, pharmacology
     *reactive oxygen metabolite: EC, endogenous compound
     *cisplatin: PD, pharmacology
     *fluorouracil: PD, pharmacology
     *cesium 137: PD, pharmacology
     *pepleomycin: PD, pharmacology
     inositol 1,4,5 trisphosphate: EC, endogenous compound
     diacylglycerol: EC, endogenous compound
     formylmethionylleucylphenylalanine
```

calcium ion: EC, endogenous compound
protein kinase c: EC, endogenous compound
phorbol 13 acetate 12 myristate
membrane enzyme: EC, endogenous compound
genistein: PD, pharmacology
staurosporine: PD, pharmacology
bromine derivative: PD, pharmacology
methionine: PD, pharmacology

L108 ANSWER 2 OF 15 MEDLINE
95404640 "Phytamins" are not ready for public consumption [news].
Eastman P. JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1995 Oct 4) 87 (19) 1430-2. Journal code: J9J. ISSN: 0027-8874. Pub. country: United States. Language: English.
CT Check Tags: Animal; Human
Antineoplastic Agents: AD, administration & dosage
Diet: AE, adverse effects
***Food, Fortified**
Isoflavones: AD, administration & dosage
Neoplasms: ET, etiology
***Neoplasms: PC, prevention & control**
Neoplasms, Experimental: PC, prevention & control
*Plants, Edible
Selenium: AD, administration & dosage
Soybeans

L108 ANSWER 3 OF 15 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95325828 EMBASE Learning how phytochemicals help fight disease. Marwick C.. Journal of the American Medical Association 274/17 (1328-1330) 1995. ISSN: 0098-7484. CODEN: JAMAAP. Pub. Country: United States. Language: English.
CT EMTAGS: **malignant neoplastic disease** (0306); epidemiology (0400); etiology (0135); prevention (0165); higher plant (0697); plant (0699); therapy (0160); mammal (0738); human (0888); nonhuman (0777); priority journal (0007); note (0063)
Medical Descriptors:
***cancer: EP, epidemiology**
***cancer: ET, etiology**
***cancer: PC, prevention**
*heart disease: EP, epidemiology
*heart disease: ET, etiology
*heart disease: PC, prevention
***dietary intake**
*phytochemistry
fruit
vegetable
cancer risk
antineoplastic activity
cancer inhibition
antioxidant activity
tea
cancer prevention
high fiber diet
grain
cereal
human
nonhuman
clinical trial
priority journal
note
Drug Descriptors:
*phenol derivative
*flavonoid
*terpene
*isothiocyanic acid derivative
garlic
ellagic acid
cigarette smoke
genistein

daidzein
quercetin
silymarin
limonene: CT, clinical trial
perillaldehyde: CT, clinical trial
nicotine
nitrosamine
ras protein

L108 ANSWER 4 OF 15 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95146305 EMBASE The relative antioxidant activities of plant-derived polyphenolic flavonoids. Rice-Evans C.A.; Miller N.J.; Bolwell P.G.; Bramley P.M.; Pridham J.B.. Free Radical Research Group, UMDS-Guy's Hospital, St Thomas's Street, London SE1 9RT, United Kingdom. Free Radical Research 22/4 (375-383) 1995. ISSN: 1071-5762. CODEN: FRARER. Pub. Country: United Kingdom. Language: English. Summary Language: English.
CT EMTAGS: chemical procedures (0107); pharmacokinetics (0194); controlled study (0197); article (0060); therapy (0160)
Medical Descriptors:
*antioxidant activity
structure activity relation
drug hydroxylation
drug structure
controlled study
article
Drug Descriptors:
*polyphenol derivative: CM, drug comparison
*polyphenol derivative: PD, pharmacology
*flavanoid: CM, drug comparison
*flavanoid: PD, pharmacology
plant extract: CM, drug comparison
plant extract: PD, pharmacology
quercetin: PD, pharmacology
cyanidin chloride: CM, drug comparison
cyanidin chloride: PD, pharmacology
trolox c: CM, drug comparison
trolox c: PD, pharmacology
kaempferol: CM, drug comparison
kaempferol: PD, pharmacology
catechin: CM, drug comparison
catechin: PD, pharmacology
epicatechin: CM, drug comparison
epicatechin: PD, pharmacology
alpha tocopherol: CM, drug comparison
ascorbic acid: CM, drug comparison
anthocyanoside derivative: CM, drug comparison
anthocyanoside derivative: PD, pharmacology
naringenin: CM, drug comparison
naringenin: PD, pharmacology
apigenin derivative: CM, drug comparison
apigenin derivative: PD, pharmacology
malvidin chloride: CM, drug comparison
malvidin chloride: PD, pharmacology
myricetin: CM, drug comparison
myricetin: PD, pharmacology
rutoside: CM, drug comparison
rutoside: PD, pharmacology
taxifolin: CM, drug comparison
taxifolin: PD, pharmacology
apigenin: CM, drug comparison
apigenin: PD, pharmacology
chrysin: CM, drug comparison
chrysin: PD, pharmacology
genistein: CM, drug comparison
genistein: PD, pharmacology
genistin: CM, drug comparison
genistin: PD, pharmacology
aurantiin: CM, drug comparison

aurantiin: PD, pharmacology
urate: CM, drug comparison
glutathione: CM, drug comparison
bilirubin: CM, drug comparison
albumin: CM, drug comparison

L108 ANSWER 5 OF 15 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95018994 EMBASE [Lower risk of breast cancer due to soya?].
BRUSTKREBSRISIKO DURCH SOJA VERMINDERT?. Thesen R.. Germany, Federal Republic of. Pharmazeutische Zeitung 140/2 (29-30) 1995. ISSN: 0031-7136. CODEN: PZSED5. Pub. Country: Germany, Federal Republic of. Language: German.
CT EMTAGS: prevention (0165); therapy (0160); mammal (0738); human (0888); female (0042); note (0063)
Medical Descriptors:
*breast cancer: PC, prevention
*breast cancer: DT, drug therapy
drug structure
nutrition
estradiol blood level
human
female
note
Drug Descriptors:
***genistein: DT, drug therapy**
estradiol: EC, endogenous compound
cholesterol: EC, endogenous compound
tamoxifen: DT, drug therapy

L108 ANSWER 6 OF 15 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95178330 EMBASE Angiogenesis and cancer metastases: Therapeutic approaches. Teicher B.A.. Dana-Farber Cancer Institute, 44 Binney Street, Boston, MA 02115, United States. Critical Reviews in Oncology/Hematology 20/1-2 (9-39) 1995. ISSN: 1040-8428. CODEN: CCRHEC. Pub. Country: Ireland. Language: English.
CT EMTAGS: malignant neoplastic disease (0306); prevention (0165); therapy (0160); mammal (0738); human (0888); nonhuman (0777); subcutaneous drug administration (0183); intraperitoneal drug administration (0178); review (0001)
Medical Descriptors:
*cancer
*metastasis: PC, prevention
*metastasis: DT, drug therapy
*angiogenesis: PC, prevention
*angiogenesis: DT, drug therapy
human
nonhuman
subcutaneous drug administration
intraperitoneal drug administration
review
Drug Descriptors:
*steroid: DT, drug therapy
*tetracycline derivative: DT, drug therapy
*heparin: DT, drug therapy
***retinoid: DT, drug therapy**
***carotenoid: DT, drug therapy**
***genistein: DT, drug therapy**
*roquinimex: DT, drug therapy
alpha2a interferon: DT, drug therapy
antineoplastic agent: DT, drug therapy
fumagillol chloroacetylcarbamate: DT, drug therapy
fumagillol chloroacetylcarbamate: CB, drug combination
tetrahydrocortisol: DT, drug therapy
tetrahydrocortisol: CB, drug combination
minocycline: DT, drug therapy
minocycline: CB, drug combination
beta carotene: DT, drug therapy
beta carotene: CB, drug combination
cisplatin: DT, drug therapy

cisplatin: CB, drug combination
fluorouracil: DT, drug therapy
fluorouracil: CB, drug combination
melphalan: DT, drug therapy
melphalan: CB, drug combination
carmustine: DT, drug therapy
carmustine: CB, drug combination
doxorubicin: DT, drug therapy
bleomycin: DT, drug therapy
calcium ion: DT, drug therapy
15 deoxyspergualin: DT, drug therapy
octreotide: DT, drug therapy
deferoxamine: DT, drug therapy
penicillamine: DT, drug therapy
anticoagulant agent: DT, drug therapy
sulindac: DT, drug therapy
sulindac: CB, drug combination
prostaglandin synthase inhibitor: DT, drug therapy
prostaglandin synthase inhibitor: CB, drug combination
diflunisal: DT, drug therapy
diflunisal: CB, drug combination
indometacin: DT, drug therapy
indometacin: CB, drug combination
mefenamic acid: DT, drug therapy
mefenamic acid: CB, drug combination
phenidone: DT, drug therapy
phenidone: CB, drug combination
unindexed drug
unclassified drug
fumagillin derivative: DT, drug therapy
cyclophosphamide: DT, drug therapy
cyclophosphamide: CB, drug combination
irsogladine maleate: DT, drug therapy
sms 995

L108 ANSWER 7 OF 15 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
94097797 EMBASE Kudzu extract shows potential for moderating alcohol abuse. AM. J. HOSP. PHARM. 51/6 (750) 1994. ISSN: 0002-9289. CODEN: AJHPA. Pub. Country: United States. Language: English.
CT EMTAGS: therapy (0160); hamsters and gerbils (0719); mammal (0738); human (0888); priority journal (0007); note (0063)
Medical Descriptors:
*alcoholism: DT, drug therapy
hamster
alcohol consumption
drug mechanism
alcohol abuse
human
priority journal
note
Drug Descriptors:
*herbal medicine: DT, drug therapy
*herbal medicine: PD, pharmacology
daidzein: DT, drug therapy
daidzein: PD, pharmacology
lithium carbonate: DT, drug therapy
bromocriptine: DT, drug therapy
buspirone: DT, drug therapy
zimeldine: DT, drug therapy

L108 ANSWER 8 OF 15 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
94164437 EMBASE Reviews and comments on alcohol research. McMillen B.A.. Ctr. for Alcohol/Drug Abuse Studies, School of Medicine, East Carolina University, Greenville, NC 27858, United States. ALCOHOL 11/3 (279-282) 1994. ISSN: 0741-8329. CODEN: ALCOEX. Pub. Country: United States. Language: English.
CT EMTAGS: diagnosis (0140); epidemiology (0400); etiology (0135); prevention (0165); therapy (0160); hamsters and gerbils (0719); mammal (0738); nonhuman (0777); animal experiment (0112); animal

model (0106); biological model (0502); controlled study (0197); intraperitoneal drug administration (0178); review (0001); enzyme (0990)
Medical Descriptors:
*alcoholism: DI, diagnosis
*alcoholism: EP, epidemiology
*alcoholism: ET, etiology
*alcoholism: PC, prevention
*alcoholism: RH, rehabilitation
alcohol consumption
enzyme inhibition
syrian hamster
nonhuman
animal experiment
animal model
controlled study
intraperitoneal drug administration
review
Drug Descriptors:
alcohol dehydrogenase: EC, endogenous compound
aldehyde dehydrogenase: EC, endogenous compound
daidzein: PD, pharmacology

L108 ANSWER 9 OF 15 MEDLINE
94346306 Potential role of dietary isoflavones in the prevention of cancer. Barnes S; Peterson G; Grubbs C; Setchell K. (Department of Biochemistry, University of Alabama at Birmingham 35294..)ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1994) 354 135-47. Journal code: 2LU. ISSN: 0065-2598. Pub. country: United States. Language: English.
CT Check Tags: Animal; Female; Human; Male; Support, Non-U.S. Gov't
Breast Neoplasms: PA, pathology
Cell Division: DE, drug effects
***Diet**
Isoflavones: AD, administration & dosage
Isoflavones: PD, pharmacology
*Isoflavones: TU, therapeutic use
Mammary Neoplasms, Experimental: CI, chemically induced
***Mammary Neoplasms, Experimental: PC, prevention & control**
Prostatic Neoplasms: PA, pathology
Rats
Rats, Sprague-Dawley
Tumor Cells, Cultured
*Vegetable Proteins
9,10-Dimethyl-1,2-benzanthracene

L108 ANSWER 10 OF 15 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
93354040 EMBASE Differentiation agents yield treatment, prevention options. Larsen N.S.. 85/23 (1900-1902) 1993. ISSN: 0027-8874. CODEN: JNCIAM. Pub. Country: United States. Language: English.
CT EMTAGS: malignant neoplastic disease (0306); therapy (0160); prevention (0165); diagnosis (0140); mammal (0738); human (0888); nonhuman (0777); oral drug administration (0181); topical drug administration (0186); note (0063)
Medical Descriptors:
*acute myeloblastic leukemia: DT, drug therapy
*uterine cervix cancer: DT, drug therapy
*uterine cervix carcinoma in situ: DT, drug therapy
*uterine cervix carcinoma in situ: PC, prevention
cell differentiation
cancer chemotherapy
cancer regression
drug resistance
hyperammonemia: DT, drug therapy
prostate cancer: DT, drug therapy
drug potentiation
tumor differentiation
cancer prevention
glioblastoma: DT, drug therapy

glioblastoma: PC, prevention
breast tumor: DT, drug therapy
breast tumor: PC, prevention
human
nonhuman
oral drug administration
topical drug administration
note
Drug Descriptors:
***retinoic acid: CB, drug combination**
***retinoic acid: DT, drug therapy**
***retinoic acid: PD, pharmacology**
*isotretinoin: CB, drug combination
*isotretinoin: DT, drug therapy
***vitamin d derivative: IT, drug interaction**
***vitamin d derivative: DT, drug therapy**
alpha interferon: CB, drug combination
alpha interferon: DT, drug therapy
fenretinide: DT, drug therapy
phenylacetic acid: DT, drug therapy
genistein: IT, drug interaction
genistein: DT, drug therapy
hexamethylenebisacetamide: IT, drug interaction
hexamethylenebisacetamide: DT, drug therapy
calcitriol: DT, drug therapy
glutamine: EC, endogenous compound

L108 ANSWER 11 OF 15 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
94019725 EMBASE Modulation of protectin (CD59 antigen) cell surface expression on human neoplastic cell lines. Sedlak J.; Hunakova L.; Duraj J.; Grofova M.; Chorvath B.. Cancer Research Institute, Slovak Academy of Sciences, 812 32 Bratislava, Slovakia. NEOPLASMA 40/6 (337-340) 1993. ISSN: 0028-2685. CODEN: NEOLA4. Pub. Country: Slovakia. Language: English. Summary Language: English.
CT EMTAGS: mammal (0738); human (0888); human tissue, cells or cell components (0111); article (0060)
Medical Descriptors:
*leukemia cell line
*tumor cell line
antigen expression
human
human cell
article
Drug Descriptors:
*cytokine: PD, pharmacology
***calcitriol: PD, pharmacology**
*membrane antigen: EC, endogenous compound
*cd59 antigen: EC, endogenous compound
phorbol ester
alpha interferon: PD, pharmacology
tumor necrosis factor alpha: PD, pharmacology
interleukin 1alpha: PD, pharmacology
genistein: PD, pharmacology
phorbol 13 acetate 12 myristate: PD, pharmacology
interleukin 6: PD, pharmacology
***retinoic acid: PD, pharmacology**

L108 ANSWER 12 OF 15 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
94051979 EMBASE Protective aspects of the Mediterranean diet. Ferro-Luzzi A.; Ghiselli A.. National Institute of Nutrition, Via Ardeatina 546, Rome, Italy. ADV. EXP. MED. BIOL. 348/- (137-144) 1993. ISSN: 0065-2598. CODEN: AEMBAP. Pub. Country: United States. Language: English.
CT EMTAGS: Europe (0402); Western Europe (4021); education (0143); mammal (0738); human (0888); priority journal (0007); review (0001)
Medical Descriptors:
***diet**
oxidative stress
eating habit

food intake
cancer risk
italy
chemical structure
health promotion
food composition
human
priority journal
review
Drug Descriptors:
*antioxidant
*bioflavonoid
quercetin
myricetin
gossypetin
biochanin a
genistein
daidzein
butein
licochalcone b
naringenin
diosmetin
rutoside

L108 ANSWER 13 OF 15 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
92151653 EMBASE Dietary phyto-oestrogens and the menopause in Japan [14]. Adlercreutz H.; Hamalainen E.; Gorbach S.; Goldin B.. Department of Clinical Chemistry, University of Helsinki, SF-00290 Helsinki, Finland. LANCET 339/8803 (1233) 1992. ISSN: 0140-6736. CODEN: LANCAO. Pub. Country: United Kingdom. Language: English.
CT EMTAGS: aged (0019); age (0020); therapy (0160); Asia (0407); mammal (0738); human (0888); male (0041); female (0042); child (0022); adult (0018); priority journal (0007); letter (0008); higher plant (0697); plant (0699)
Medical Descriptors:
*menopause
***diet supplementation**
japan
urinalysis
human
male
female
child
adult
priority journal
letter
Drug Descriptors:
*estrogen: EC, endogenous compound
***genistein: EC, endogenous compound**
*isoflavonoid: PD, pharmacology
*herb: PD, pharmacology

L108 ANSWER 14 OF 15 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
89250070 EMBASE Sixth International Symposium on SHR and Related Studies organized by the cardiovascular center at the university of Iowa, Iowa City, Iowa, May 22-24, 1989. Scriabine A.. United States. CARDIOVASC. DRUG REV. 7/3 (210-213) 1989. ISSN: 0897-5957. CODEN: CDREEA. Pub. Country: United States. Language: English.
CT EMTAGS: rat (0733); cardiovascular system (0920); etiology (0135); animal model (0106); bone (0962); peripheral vascular system (0923); heredity (0137); short survey (0002); human (0888); nonhuman (0777)
Medical Descriptors:
*spontaneously hypertensive rat
*hypertension: ET, etiology
*animal model
diet
osteoporosis
atherogenesis
blood pressure

heredity
Drug Descriptors:
arotinolol
propranolol
pindolol
idebenone
genistein
solcoseryl
budralazine
nifedipine
nicardipine
isradipine
1,4 dihydro 2,6 dimethyl 5 nitro 4 [2 (trifluoromethyl)phenyl] 3 pyridinecarboxylic acid methyl ester
ex 89
indometacin
n methyl dextro aspartic acid
kainic acid
captopril
1 [6 amino 2 [hydroxy(4 phenylbutyl)phosphinyloxy] 1 oxohexyl]proline
labetalol

L108 ANSWER 15 OF 15 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
87059814 EMBASE Determination of urinary lignans and phytoestrogen metabolites, potential antiestrogens and anticarcinogens, in urine of women on various habitual diets. Adlercreutz H.; Fotsis T.; Bannwart C.; et al.. Department of Clinical Chemistry, University of Helsinki, Meilahti Hospital, SF-00290 Helsinki, Finland. J. STEROID BIOCHEM. 25/5B (791-797) 1986. CODEN: JSTBBK. Pub. Country: United Kingdom. Language: English.
CT EMTAGS: priority journal (0007); drug analysis (0190); drug urine levels (0192); pharmacokinetics (0194); **malignant neoplastic disease** (0306); oral drug administration (0181); abstract report (0005); chemical procedures (0107); human (0888); etiology (0135); cattle (0707); sheep (0737); rat (0733); age (0020); sex difference (0040); ethnic or racial aspects (0050); epidemiology (0400); geographical aspects (0401); urinary tract (0950); female genital system (0957); human tissue, cells or cell components (0111); animal experiment (0112); animal tissue, cells or cell components (0105); higher plant (0697)
Medical Descriptors:
*drug determination
*drug urine level
*drug metabolism
*drug receptor binding
*drug interaction
*gas chromatography
*mass spectrometry
***diet**
***macrobiotic diet**
***breast cancer**
*lignan
*phytoestrogen
*antiestrogen agent
*antineoplastic agent
***dietary intake**
*vegetarian
*enterolactone
*enterodiol
***daidzein**
*equol
*norangelosin
*matairesinol
urine
protection
formononetin
oxytetracycline

=> d l109 1-79 cbib ab ct

L109 ANSWER 1 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
96131474 EMBASE Effects of hormonal therapies and dietary soy phytoestrogens on vaginal cytology in surgically postmenopausal macaques. Cline J.M.; Paschold J.C.; Anthony M.S.; Obasanjo I.O.; Adams M.R.. Department of Comparative Medicine, Bowman Gray School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157-1040, United States. Fertility and Sterility 65/5 (1031-1035) 1996. ISSN: 0015-0282. CODEN: FESTAS. Pub. Country: United States. Language: English. Summary Language: English.

AB Objective: To evaluate the effects of conjugated equine estrogens, medroxyprogesterone acetate (MPA), conjugated equine estrogens combined with MPA, tamoxifen, and soybean estrogens on vaginal cytology in surgically postmenopausal cynomolgus macaques (Macaca fascicularis). Design: Randomized long-term experimental trial. Setting: Cytologic samples were taken from animals in two long-term randomized studies of the effects of hormonal and dietary effects on atherosclerosis. Patients: Surgically postmenopausal cynomolgus macaques. Interventions: Conjugated equine estrogens, MPA, conjugated equine estrogens combined with MPA, tamoxifen, and soybean estrogens were given via the diet, at doses scaled from those given to women. Main Outcome Measure: Vaginal cytologic maturation index. Results: Conjugated equine estrogens elicited a marked maturation effect, which was antagonized partially by the addition of MPA. Tamoxifen produced a lesser estrogenic response. The cytologic pattern in animals given soybean estrogens or MPA alone did not differ from that of controls. Conclusion: Soybean estrogens at the doses given do not exert an estrogenic effect on the vagina of macaques. Conjugated equine estrogens are potent inducers of vaginal keratinization in this model; tamoxifen has a lesser effect. Medroxyprogesterone acetate partially antagonizes the effects of conjugated equine estrogens, and has no effect when given alone. The results support the possibility that soybean estrogens may be a 'tissue-selective' estrogen with minimal effects on the reproductive tract.

CT EMTAGS: age (0020); therapy (0160); diagnosis (0140); cytology (0332); mammal (0738); higher plant (0697); plant (0699); nonhuman (0777); female (0042); animal model (0106); biological model (0502); controlled study (0197); animal tissue, cells or cell components (0105); oral drug administration (0181); priority journal (0007); article (0060)
Medical Descriptors:
*postmenopause
*estrogen therapy
*vagina cytology
macaca
soybean
dietary intake
hormone substitution
tissue specificity
estrogen blood level
progesterone blood level
hormone action
dose response
postmenopause osteoporosis
atherosclerosis
ovariectomy
nonhuman
female
animal model
controlled study
animal cell
oral drug administration
priority journal
article
Drug Descriptors:
*conjugated estrogen: CB, drug combination
*conjugated estrogen: CM, drug comparison

*conjugated estrogen: DO, drug dose
*conjugated estrogen: PD, pharmacology
*medroxyprogesterone acetate: CB, drug combination
*medroxyprogesterone acetate: CM, drug comparison
*medroxyprogesterone acetate: DO, drug dose
*medroxyprogesterone acetate: PD, pharmacology
*tamoxifen: CB, drug combination
*tamoxifen: CM, drug comparison
*tamoxifen: DO, drug dose
*tamoxifen: PD, pharmacology
*phytoestrogen: CB, drug combination
*phytoestrogen: CM, drug comparison
*phytoestrogen: CR, drug concentration
*phytoestrogen: DO, drug dose
*phytoestrogen: PD, pharmacology
*soybean protein: CB, drug combination
*soybean protein: CM, drug comparison
*soybean protein: CR, drug concentration
*soybean protein: DO, drug dose
*soybean protein: PD, pharmacology
estradiol: EC, endogenous compound
progesterone: EC, endogenous compound
isoflavone: CB, drug combination
isoflavone: CM, drug comparison
isoflavone: CR, drug concentration
isoflavone: DO, drug dose
isoflavone: PD, pharmacology
genistein: CB, drug combination
genistein: CM, drug comparison
genistein: CR, drug concentration
genistein: DO, drug dose
genistein: PD, pharmacology
daidzein: CB, drug combination
daidzein: CM, drug comparison
daidzein: CR, drug concentration
daidzein: DO, drug dose
daidzein: PD, pharmacology
estrogen receptor

L109 ANSWER 2 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
96060695 EMBASE Reciprocal modulation of ATP-sensitive K+ channel activity in rat ventricular myocytes by phosphorylation of tyrosine and serine/threonine residues. Kwak Y.G.; Park S.K.; Cho K.P.; Chae S.W.. Department of Pharmacology, Chonbuk National University, Medical School, Chonju 560-182, Korea, Republic of. Life Sciences 58/11 (897-904) 1996. ISSN: 0024-3205. CODEN: LIFSAK. Pub. Country: United States. Language: English. Summary Language: English.

AB The modulation of ATP-sensitive K+ channel (K(ATP)) activity by specific phosphorylation or dephosphorylation of tyrosine and serine/threonine, residues was examined in rat ventricular myocytes using the inside-out patch configuration of the patch clamp technique. The run-down process was suppressed by okadaic acid but accelerated by sodium orthovanadate. After run-down of the channels, the ATP-induced reactivation was blocked by H-7, but enhanced by genistein. The channel activity was decreased by protein phosphatase 2A. However, the activity of partially run-down channels was increased by protein tyrosine phosphatase 1B. Our results suggest that K(ATP) channel activity can be inhibited by phosphorylation of tyrosine residues and stimulated by phosphorylation of serine/threonine residues.

CT EMTAGS: cardiovascular system (0920); heart (0921); musculoskeletal system (0960); muscle (0961); chemical procedures (0107); apparatus, equipment and supplies (0510); nonhuman (0777); rat (0733); mammal (0738); controlled study (0197); animal tissue, cells or cell components (0105); article (0060); enzyme (0990)
Medical Descriptors:
*heart muscle cell
*potassium channel
*protein phosphorylation

heart ventricle
patch clamp
dephosphorylation
membrane current
nonhuman
rat
controlled study
animal cell
article
Drug Descriptors:
*tyrosine
*serine
***threonine**
adenosine triphosphate: PD, pharmacology
okadaic acid: PD, pharmacology
orthovanadic acid: PD, pharmacology
1 (5 isoquinolinesulfonyl) 2 methylpiperazine: PD, pharmacology
genistein: PD, pharmacology
phosphoprotein phosphatase 2a
protein tyrosine phosphatase 1b
phosphoprotein phosphatase
unclassified drug

L109 ANSWER 3 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
96106257 EMBASE A diet high in wheat fiber decreases the bioavailability of soybean isoflavones in a single meal fed to women. Tew B.-Y.; Xu X.; Wang H.-J.; Murphy P.A.; Hendrich S.. Dept. of Food Sci./Human Nutrition, Iowa State University, Ames, IA 50011, United States. Journal of Nutrition 126/4 (871-877) 1996. ISSN: 0022-3166. CODEN: JONUAI. Pub. Country: United States. Language: English. Summary Language: English.

AB The absorption of some dietary components may be inhibited by dietary fiber. To study the effect of dietary fiber on the bioavailability of isoflavones, seven healthy women were randomly assigned in a crossover design to a control diet containing 15 g dietary fiber or a wheat fiber-supplemented diet containing 40 g dietary fiber, both fed with a single dose of 0.9 mg isoflavones/kg body weight from tofu or texturized vegetable protein (TVP). The fiber-rich diet produced 55% lower plasma genistein at 24 h after soy dosing ($P < 0.05$) and reduced total urinary genistein by 20% ($P < 0.03$). Urinary daidzein was not significantly related to fiber intake. Highly insoluble, dietary wheat fiber reduced the absorption of genistein probably by its bulking effect and hydrophobic binding to this compound. Urinary genistein was greater by 23% after tofu than after TVP consumption ($P < 0.02$), but the percentage of ingested genistein recovered in urine was not affected by soy product intake. The higher urinary genistein after tofu consumption compared with TVP was apparently due to differences in amount of genistein between these soy foods, not the different forms of genistein present in these two soy food products.

CT EMTAGS: therapy (0160); higher plant (0697); plant (0699); mammal (0738); human (0888); female (0042); human experiment (0104); normal human (0800); controlled study (0197); human tissue, cells or cell components (0111); adult (0018); article (0060); pharmacokinetics (0194)
Medical Descriptors:
*high fiber diet
***diet supplementation**
bioavailability
wheat
soybean
intestine absorption
food composition
urinary excretion
high performance liquid chromatography
human
female
human experiment
normal human

controlled study
human tissue
human cell
adult
article
Drug Descriptors:
***genistein: EC, endogenous compound**
***daidzein: EC, endogenous compound**
*isoflavone: PK, pharmacokinetics
*vegetable protein: EC, endogenous compound

L109 ANSWER 4 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
96061847 EMBASE Flavonoids, potent inhibitors of the human P-form phenolsulfotransferase: Potential role in drug metabolism and chemoprevention. Eaton E.A.; Walle U.K.; Lewis A.J.; Hudson T.; Wilson A.A.; Walle T.. DCMPET, Medical University of South Carolina, 171 Ashley Avenue, Charleston, SC 29425, United States. Drug Metabolism and Disposition 24/2 (232-237) 1996. ISSN: 0090-9556. CODEN: DMDSAI. Pub. Country: United States. Language: English. Summary Language: English.

AB The common dietary constituent quercetin was a potent inhibitor of sulfoconjugation of acetaminophen and minoxidil by human liver cytosol, partially purified P-form phenolsulfotransferase (PST), and recombinant P- form PST, with IC50 values of 0.025-0.095 .mu.M. Quercetin inhibition of acetaminophen was noncompetitive with respect to acceptor substrate, with a K(i) value of 0.067 .mu.M. A number of other flavonoids, such as fisetin, galangin, myricetin, kaempferol, chrysin, and apigenin, were also potent inhibitors of P-form PST-mediated sulfation, with IC50 values < 1 .mu.M. Studies of structural analogs indicated the flavonoid 7-hydroxyl group as particularly important for potent inhibition. Potential human metabolites of quercetin were poor inhibitors. Curcumin, genistein, and ellagic acid (other polyphenolic natural products) were also inhibitors of P-form PST, with IC50 values of 0.38-34.8 .mu.M. Quercetin was also shown to inhibit sulfoconjugation by the human hepatoma cell line Hep G2. Although less potent in this intact cell system (IC50 2-5 .mu.M), quercetin was still more potent than 2,6-dichloro-4-nitrophenol, the classical P-form PST inhibitor that has been shown to be an inhibitor also in vivo. These observations suggest the potential for clinically important drug interactions, as well as a possible role for flavonoids as chemopreventive agents in sulfation-induced carcinogenesis.

CT EMTAGS: chemical procedures (0107); pharmacokinetics (0194); therapy (0160); prevention (0165); mammal (0738); human (0888); human tissue, cells or cell components (0111); priority journal (0007); article (0060); enzyme (0990)
Medical Descriptors:
*drug sulfation
*enzyme inhibition
*cancer prevention
hepatoma cell
liver cytosol
dietary intake
drug metabolism
drug structure
drug effect
concentration response
drug potency
human
human cell
priority journal
article
Drug Descriptors:
*paracetamol: PK, pharmacokinetics
*minoxidil: PK, pharmacokinetics
*flavonoid: AN, drug analysis
*flavonoid: CM, drug comparison
*flavonoid: PD, pharmacology
*quercetin: AN, drug analysis

*quercetin: CM, drug comparison
*quercetin: PD, pharmacology
*2,6 dichloro 4 nitrophenol: CM, drug comparison
*2,6 dichloro 4 nitrophenol: PD, pharmacology
*aryl sulfotransferase: EC, endogenous compound
fisetin: AN, drug analysis
fisetin: CM, drug comparison
fisetin: PD, pharmacology
galangin: AN, drug analysis
galangin: CM, drug comparison
galangin: PD, pharmacology
myricetin: AN, drug analysis
myricetin: CM, drug comparison
myricetin: PD, pharmacology
kaempferol: AN, drug analysis
kaempferol: CM, drug comparison
kaempferol: PD, pharmacology
chrysin: AN, drug analysis
chrysin: CM, drug comparison
chrysin: PD, pharmacology
apigenin: AN, drug analysis
apigenin: CM, drug comparison
apigenin: PD, pharmacology
benzopyran derivative: AN, drug analysis
benzopyran derivative: CM, drug comparison
benzopyran derivative: PD, pharmacology
curcumin: AN, drug analysis
curcumin: CM, drug comparison
curcumin: PD, pharmacology
genistein: AN, drug analysis
genistein: CM, drug comparison
genistein: PD, pharmacology
ellagic acid: AN, drug analysis
ellagic acid: CM, drug comparison
ellagic acid: PD, pharmacology

L109 ANSWER 5 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
96071891 EMBASE Synergistic and selective stimulation of gelatinase B production in macrophages by lipopolysaccharide, trans-retinoic acid and CGP 41251, a protein kinase C regulator. Houde M.; Tremblay P.; Masure S.; Opdenakker G.; Oth D.; Mandeville R.. Institut Armand-Frappier, Centre Recherches en Immunologie, Laval, Que. H7N 4Z3, Canada. Biochimica et Biophysica Acta - Molecular Cell Research 1310/2 (193-200) 1996. ISSN: 0167-4889. CODEN: BAMRDP. Pub. Country: Netherlands. Language: English. Summary Language: English.

AB The production of gelatinase B by macrophages is relevant in the immunological and migratory functions of macrophages. CGP 41251, an inhibitor of protein kinase C (PKC), was found to stimulate the expression of gelatinase B in macrophages, as shown by the study of two different monocytic/macrophagic cell lines, mouse RAW 264.7 and human THP-1 cells. When human monocytes and rat peritoneal macrophages were treated with CGP 41251, insignificant increases of 10 and 258 were obtained. This can possibly be due to the presence of contaminating cells in these two enriched populations, since the CGP 41251 treatment of non-macrophagic cell lines inhibited their PMA-induced gelatinase B production. Taken together, these results suggest that the stimulatory effect of CGP 41251 is specific to cells of the monocytic lineage. Using RAW 264.7 cells as a model, the effect of CGP 41251 is additive to that obtained using lipopolysaccharide (LPS) and phorbol 12-myristate 13-acetate (PMA), as revealed by gelatin zymography and Northern blot analysis. The stimulatory effect of CGP 41251 on gelatinase B production in RAW 264.7 was: (a) inhibited by calphostin C (as is the LPS-induced response), indicating a PKC-dependence; (b) inhibited by dexamethasone (as opposed to the LPS-induced response); and (c) enhanced by addition of trans-retinoic acid (RA), In fact, RA can induce gelatinase B production, either alone or in synergy with LPS and/or CGP 41251, since the combination of the three agents gives the highest gelatinase B response, at both the protein and the mRNA

levels. This represents an important observation considering that RA is now being tested as an anti-cancer agent and proposed for prevention studies.

CT EMTAGS: reticuloendothelial system (0924); blood and hemopoietic system (0927); genetic engineering and gene technology (0108); heredity (0137); cell, tissue or organ culture (0103); mammal (0738); human (0888); nonhuman (0777); mouse (0727); rat (0733); controlled study (0197); human tissue, cells or cell components (0111); animal tissue, cells or cell components (0105); priority journal (0007); article (0060); enzyme (0990); therapy (0160)

Medical Descriptors:
*macrophage
*enzyme activity
cell line
monocyte
peritoneum macrophage
gene expression
northern blotting
cell culture
human
nonhuman
mouse
rat
controlled study
human cell
animal cell
priority journal
article

Drug Descriptors:
*gelatinase b: EC, endogenous compound
*cgp 41251: CB, drug combination
*cgp 41251: CM, drug comparison
*cgp 41251: DO, drug dose
*cgp 41251: PD, pharmacology
*lipopolysaccharide: CB, drug combination
*lipopolysaccharide: CM, drug comparison
*lipopolysaccharide: IT, drug interaction
*lipopolysaccharide: PD, pharmacology
***retinoic acid: CB, drug combination**
***retinoic acid: CM, drug comparison**
***retinoic acid: IT, drug interaction**
***retinoic acid: PD, pharmacology**
*phorbol 13 acetate 12 myristate: CB, drug combination
*phorbol 13 acetate 12 myristate: CM, drug comparison
*phorbol 13 acetate 12 myristate: PD, pharmacology
calphostin c: CB, drug combination
calphostin c: CM, drug comparison
calphostin c: IT, drug interaction
dexamethasone: CB, drug combination
dexamethasone: CM, drug comparison
dexamethasone: IT, drug interaction
protein kinase c: EC, endogenous compound
nitric oxide: EC, endogenous compound
okadaic acid: CM, drug comparison
okadaic acid: PD, pharmacology
herbimycin a: CM, drug comparison
herbimycin a: PD, pharmacology
genistein: CM, drug comparison
genistein: PD, pharmacology
egtazic acid: CM, drug comparison
egtazic acid: PD, pharmacology
messenger rna: EC, endogenous compound
calcimycin: CM, drug comparison
calcimycin: PD, pharmacology
kt 5823: CB, drug combination
kt 5823: PD, pharmacology
unclassified drug
kt 5720: CM, drug comparison
kt 5720: PD, pharmacology

L109 ANSWER 6 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
96034970 EMBASE Absorption and excretion of the soy isoflavone genistein in rats. King R.A.; Broadbent J.L.; Head R.J.. CSIRO Division of Human Nutrition, Adelaide, SA 5000, Australia. Journal of Nutrition 126/1 (176-182) 1996. ISSN: 0022-3166. CODEN: JONUAI. Pub. Country: United States. Language: English. Summary Language: English.

AB Rodent models have been used to study the anticarcinogenic properties of the soy isoflavones, particularly genistein, but there is little information regarding the pharmacokinetics of the absorption and excretion of genistein. In this study, rats were given a single oral dose of genistein (20 mg/kg body weight) or an equivalent close of its glycone forms, as an isoflavone-rich soy extract. Concentrations of genistein were measured in plasma, urine and feces at intervals up to 48 h after dosing. Plasma genistein concentration at 2 h after dosing was 11.0 .+-. 2.3 .mu.mol/L in genistein-treated rats compared with 4.93 .+-. 0.22 .mu.mol/L (P = 0.025) in soy extract-treated rats, but there were no significant differences at 8 h and later times. The mean urinary excretion rate during the first 2 h after dosing was more than 10 times higher in the genistein group compared with the soy extract group (0.27 .+-. 0.08 .mu.mol/h and 0.020 .+-. 0.011 .mu.mol/h, respectively, P = 0.017) but the percentage of dose recovered in urine over 48 h was not different between groups (19.9 .+-. 2.4% genistein treated; 17.5 .+-. 1.1% soy extract treated). There were no significant differences between groups in the recovery of genistein in feces (21.9 .+-. 2.8% and 21.1 .+-. 2.5% of dose, respectively). Only 6.1 .+-. 0.9% of the daidzein from the soy extract was recovered in the feces. The results suggest that the extent of absorption of genistein is similar for the glycone and aglycone forms. Although higher initial plasma concentrations may be achieved with the aglycone, similar long-term concentrations exist for both forms of isoflavone.

CT EMTAGS: pharmacokinetics (0194); higher plant (0697); plant (0699); nonhuman (0777); male (0041); rat (0733); mammal (0738); animal experiment (0112); controlled study (0197); animal tissue, cells or cell components (0105); oral drug administration (0181); article (0060)

Medical Descriptors:
*drug absorption
*drug excretion
drug blood level
drug feces level
drug urine level
soybean
nonhuman
male
rat
animal experiment
controlled study
animal tissue
oral drug administration
article

Drug Descriptors:
***genistein: CR, drug concentration**
***genistein: PK, pharmacokinetics**
*isoflavone: CR, drug concentration
*isoflavone: PK, pharmacokinetics
*plant extract
***daidzein**
*equol

L109 ANSWER 7 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
96074873 EMBASE Mechanisms involved in the spasmolytic effect of extracts from Sabal serrulata fruit on smooth muscle. Gutierrez M.; Garcia de Boto M.J.; Cantabrana B.; Hidalgo A.. Laboratorio de Farmacologia, Departamento de Medicina, Facultad de Medicina, C/Julian Claveria s/n, 33006 Oviedo, Spain. General Pharmacology

27/1 (171-176) 1996. ISSN: 0306-3623. CODEN: GEPHDP. Pub. Country: United States. Language: English. Summary Language: English.

AB 1. The effects of two extracts from Sabal serrulata fruits [total lipidic (L) and saponifiable (S)] on smooth muscle contractions have been assayed. 2. Both extracts (0.1-1 mg/ml) relaxed the tonic contraction induced by norepinephrine (30 nM) on rat aorta [EC50, 0.53 .+-. 0.05 mg/ml (L) and 0.5 .+-. 0.04 mg/ml (S)] and by KCl (60 mM) on rat uterus. The Sabal extracts (0.3-1 mg/ml) also antagonized the dose-response curve of contractions induced by acetylcholine (0.1-100 .mu.M) on urinary bladder. 3. dL-Propranolol (1 .mu.M) but not the inactive (R)-(+)-propranolol (1 .mu.M) potentiated the Sabal extracts relaxant effect by lowering the EC50 (0.35 .+-. 0.2 vs 0.20 .+-. 0.01 mg/ml for L and 0.43 .+-. 0.02 vs 0.19 .+-. 0.02 mg/ml, P < 0.01, for S extract). 4. Cycloheximide (10 .mu.g/ml) antagonized the effect of extracts from Sabal. However, actinomycin D (5 .mu.g/ml) significantly (P .ltoreq. 0.01) antagonized the effect of the total lipidic extract without modifying that of the saponifiable extract. 5. The relaxant effect of both extracts was not modified by the tyrosine kinase inhibitor genistein (10 .mu.M) or the ornithine decarboxylase inhibitor .alpha.-difluoromethyl-ornithine (10 mM).

CT EMTAGS: therapy (0160); higher plant (0697); plant (0699); cardiovascular system (0920); great blood vessel (0922); female genital system (0957); urinary tract (0950); bladder (0952); nonhuman (0777); rat (0733); mammal (0738); controlled study (0197); animal tissue, cells or cell components (0105); male (0041); female (0042); priority journal (0007); article (0060)
Medical Descriptors:
*smooth muscle contraction
*spasmolysis
fruit
drug mechanism
concentration response
drug inhibition
drug potentiation
aorta
uterus
bladder
enantiomer
nonhuman
rat
controlled study
animal tissue
male
female
priority journal
article
Drug Descriptors:
*sabal: PD, pharmacology
*sabal: IT, drug interaction
*plant extract: PD, pharmacology
*plant extract: IT, drug interaction
*spasmolytic agent: PD, pharmacology
*spasmolytic agent: IT, drug interaction
noradrenalin: PD, pharmacology
noradrenalin: IT, drug interaction
potassium chloride: PD, pharmacology
potassium chloride: IT, drug interaction
acetylcholine: PD, pharmacology
acetylcholine: IT, drug interaction
propranolol: PD, pharmacology
propranolol: IT, drug interaction
cycloheximide: PD, pharmacology
cycloheximide: IT, drug interaction
dactinomycin: PD, pharmacology
dactinomycin: IT, drug interaction
genistein: PD, pharmacology
protein tyrosine kinase inhibitor: PD, pharmacology
eflornithine: PD, pharmacology
ornithine decarboxylase inhibitor: PD, pharmacology

haloperidol: PD, pharmacology

L109 ANSWER 8 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
96098124 EMBASE Analysis of plasma isoflavones by reversed-phase HPLC-multiple reaction ion monitoring-mass spectrometry. Coward L.; Kirk M.; Albin N.; Barnes S.. Dept. of Pharmacology and Toxicology, UAB Comprehensive Cancer Center, University of Alabama, Birmingham, AL 35294-0019, United States. Clinica Chimica Acta 247/1-2 (121-142) 1996. ISSN: 0009-8981. CODEN: CCATAR. Pub. Country: Netherlands. Language: English. Summary Language: English.

AB A HPLC-MS procedure for the rapid, sensitive and specific measurement of the isoflavones, daidzein, dihydrodaidzein, O-desmethylangolensin and genistein, in human plasma has been developed. Synthetic radiolabeled genistein conjugates were used for evaluation of optimum conditions for solid phase extraction. Biochanin A was added to plasma as a recovery marker for isoflavones and phenolphthalein glucuronide and 4-methylumbelliferone sulfate were added to ensure completeness of hydrolysis with .beta.-glucuronidase/sulfatase. Isoflavones in plasma extracts were separated using an isocratic HPLC method and analyzed by negative ion multiple reaction ion monitoring-mass spectrometry using a heated nebulizer-atmospheric pressure chemical ionization interface. Using plasma samples from four subjects consuming two servings a day of an isolated soy protein beverage for 14 days, the mean plasma genistein and daidzein concentrations were 556 and 345 nM, respectively. Within assay and between assay coefficients of variation for measurement of daidzein and genistein in five aliquots of the same plasma sample were 8.51% and 7.76%, and 5.98% and 6.12%, respectively.

CT EMTAGS: methodology (0130); mammal (0738); human (0888); normal human (0800); human tissue, cells or cell components (0111); priority journal (0007); article (0060)
Medical Descriptors:
*blood analysis
*reversed phase high performance liquid chromatography
*mass spectrometry
technique
diet
human
normal human
human tissue
priority journal
article
Drug Descriptors:
*isoflavone: EC, endogenous compound
***daidzein: EC, endogenous compound**
***genistein: EC, endogenous compound**

L109 ANSWER 9 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
96082488 EMBASE [Nutritional interest of flavonoids]. INTERET NUTRITIONNEL DES FLAVONOIDES. Remesy C.; Manach C.; Demigne C.; Texier O.; Regerat F.. Ctr. de Recherche/Nutrition Humaine, I.N.R.A., Unite des Maladies Metaboliques, 63122 St-Genes-Champanelle, France. Medecine et Nutrition 32/1 (17-27) 1996. ISSN: 0398-7604. CODEN: MENUDI. Pub. Country: France. Language: French. Summary Language: French; English.

AB Polyphenols represent a complex group of compounds including several categories such as 4-oxo-flavonoids, anthocyanins and tannins. Some of these molecules are present in substantial amounts in various beverages and in plant foods (fruits, vegetables...), and several investigations have established that they were liable to cross the intestinal barrier in mammals. Significant concentrations of flavonoid or polyphenol metabolites are likely to circulate in blood plasma in humans, and it appears thus important to assess their potential biological effects. Some interesting properties have already been reported, especially as to 4-oxo-flavonoids: they have antioxidizing and metal-complexing properties, and they are liable to modulate the activity of enzymes governing important cell functions. By protecting L.D.L. from oxidative alterations and by

affecting platelet functions and plasma cholesterol, flavonoids might play a protective role against atherosclerosis. Some 4-oxo-flavonoids (quercetin, genistein...) show antiproliferative properties in vitro and inhibit the development of chimio-induced cancers in animal models. Thus, together with other micronutriments, their occurence in fruits and legumes could explain the preventive effects towards cancer risk of plant foods. Isoflavones which present a phytoestrogenic activity could be more specifically involved in the prevention of breast cancer risk. Further investigations are required to determine the actual bioavailability of the different classes of flavonoids, and to fully understand the underlying mechanisms of their biological effects.

CT EMTAGS: **malignant neoplastic disease** (0306); prevention (0165); higher plant (0697); plant (0699); mammal (0738); human (0888); review (0001)

Medical Descriptors:
*antioxidant activity
***cancer: PC, prevention**
***breast cancer: PC, prevention**
*coronary artery disease
diet
vegetable
fruit
human
review

Drug Descriptors:
*flavonoid: PD, pharmacology
*anthocyanin: PD, pharmacology
*tannin: PD, pharmacology
*low density lipoprotein: EC, endogenous compound
apigenin: PD, pharmacology
baicalein: PD, pharmacology
diosmetin: PD, pharmacology
luteolin: PD, pharmacology
fisetin: PD, pharmacology
kaempferol: PD, pharmacology
morin: PD, pharmacology
myricetin: PD, pharmacology
quercetin: PD, pharmacology
daidzein: PD, pharmacology
genistein: PD, pharmacology
taxifolin: PD, pharmacology
hesperetin: PD, pharmacology
liquiritigenin: PD, pharmacology
naringenin: PD, pharmacology

L109 ANSWER 10 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.

96041445 EMBASE Effect of dietary genistein on antioxidant enzyme activities in SENCAR mice. Cai Q.; Wei H.. Dept. of Dermatology, Mount Sinai School of Medicine, 5 East 98th St., New York, NY 10029, United States. Nutrition and Cancer 25/1 (1-7) 1996. ISSN: 0163-5581. CODEN: NUCADQ. Pub. Country: United States. Language: English. Summary Language: English.

AB Dietary administration of the soybean isoflavone genistein (50 and 250 ppm) for 30 days significantly increases the activities of antioxidant enzymes in various organs of SENCAR mice. Feeding a 250-ppm genistein diet to SENCAR mice significantly increases the activities of catalase in small intestine, liver, and kidney, the activities of superoxide dismutase and glutathione peroxidase in skin, and the activity of glutathione reductase in skin and small intestine. Feeding 50 ppm genistein to SENCAR mice results in elevated catalase activity in the small intestine and increases glutathione- S-transferase activities in skin, small intestine, liver, kidney, and lung. Dietary genistein's greatest enhancement of antioxidant enzyme activities occurred in skin and small intestine. Our results suggest that dietary genistein enhances the activities of antioxidant enzymes in various organs, which may be a mechanism(s) of genistein's chemopreventive action.

CT EMTAGS: higher plant (0697); plant (0699); skin, hair, nails and

sweat glands (0980); digestive system (0935); small intestine (0941); liver (0946); nonhuman (0777); mouse (0727); mammal (0738); animal experiment (0112); animal model (0106); biological model (0502); controlled study (0197); oral drug administration (0181); article (0060); enzyme (0990)
Medical Descriptors:
***dietary intake**
enzyme activity
soybean
antineoplastic activity
lipid peroxidation
enzyme inhibition
drug effect
skin
small intestine
liver microsome
nonhuman
mouse
animal experiment
animal model
controlled study
oral drug administration
article
Drug Descriptors:
***genistein: AD, drug administration**
***genistein: PD, pharmacology**
*antioxidant
catalase

L109 ANSWER 11 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95280618 EMBASE Daidzin suppresses ethanol consumption by Syrian golden hamsters without blocking acetaldehyde metabolism. Keung W.-M.; Lazo O.; Kunze L.; Vallee B.L.. Biochem./Biophysical Sci./Med. Ctr., Harvard Medical School, 250 Longwood Avenue, Boston, MA 02115, United States. Proceedings of the National Academy of Sciences of the United States of America 92/19 (8990-8993) 1995. ISSN: 0027-8424. CODEN: PNASA6. Pub. Country: United States. Language: English. Summary Language: English.

AB Daidzin is a potent, selective, and reversible inhibitor of human mitochondrial aldehyde dehydrogenase (ALDH) that suppresses free-choice ethanol intake by Syrian golden hamsters. Other ALDH inhibitors, such as disulfiram (Antabuse) and calcium citrate carbimide (Temposil), have also been shown to suppress ethanol intake of laboratory animals and are thought to act by inhibiting the metabolism of acetaldehyde produced from ingested ethanol. To determine whether or not daidzin inhibits acetaldehyde metabolism in vivo, plasma acetaldehyde in daidzin-treated hamsters was measured after the administration of a test dose of ethanol. Daidzin treatment (150 mg/kg per day i.p. for 6 days) significantly suppresses (>70%) hamster ethanol intake but does not affect overall acetaldehyde metabolism. In contrast, after administration of the same ethanol dose, plasma acetaldehyde concentration in disulfiram-treated hamsters reaches 0.9 mM, 70 times higher than that of the control. In vitro, daidzin suppresses hamster liver mitochondria-catalyzed acetaldehyde oxidation very potently with an IC50 value of 0.4 .mu.M, which is substantially lower than the daidzin concentration (70 .mu.M) found in the liver mitochondria of daidzin-treated hamsters. These results indicate that (i) the action of daidzin differs from that proposed for the classic, broad-acting ALDH inhibitors (e.g., disulfiram), and (ii) the daidzin-sensitive mitochondrial ALDH is not the one and only enzyme that is essential for acetaldehyde metabolism in golden hamsters.

CT EMTAGS: hamsters and gerbils (0719); mammal (0738); digestive system (0935); liver (0946); nonhuman (0777); animal experiment (0112); controlled study (0197); animal tissue, cells or cell components (0105); intraperitoneal drug administration (0178); priority journal (0007); article (0060); enzyme (0990)
Medical Descriptors:
*alcoholism

syrian hamster
alcohol consumption
alcohol metabolism
drug mechanism
dose response
liver metabolism
liver mitochondrion
nonhuman
animal experiment
controlled study
animal tissue
intraperitoneal drug administration
priority journal
article
Drug Descriptors:
*alcohol: DO, drug dose
*acetaldehyde
*mitochondrial enzyme: EC, endogenous compound
*aldehyde dehydrogenase: EC, endogenous compound
***daidzein: AD, drug administration**
***daidzein: DV, drug development**
***daidzein: DO, drug dose**
***daidzein: PD, pharmacology**
disulfiram: PD, pharmacology
calcium carbimide citrate: PD, pharmacology
urethan: AD, drug administration
urethan: DO, drug dose

L109 ANSWER 12 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95307376 EMBASE Soluble interleukin-6 (IL-6) receptor in the sera of pregnant women forms a complex with IL-6 and augments human chorionic gonadotropin production by normal human trophoblasts through binding to the IL-6 signal transducer. Matsuzaki N.; Neki R.; Sawai K.; Shimoya K.; Okada T.; Sakata M.; Saji F.; Koishihara Y.; Ida N.. Department of Obstetrics/Gynecology, Osaka University Medical School, 2-2 Yamadaoka, Suita, Osaka 565, Japan. Journal of Clinical Endocrinology and Metabolism 80/10 (2912-2917) 1995. ISSN: 0021-972X. CODEN: JCEMAZ. Pub. Country: United States. Language: English. Summary Language: English.

AB To study the role of soluble interleukin 6 receptor (sIL-6R) during pregnancy, sIL-6R levels in the sera of pregnant women in the first, second, and third trimesters were determined and found to remain unchanged during pregnancy, but were significantly higher than those in nonpregnant women in the follicular, ovulatory, and luteal phases of the menstrual cycle ($P < 0.001$). IL-6 levels, however, in the sera of pregnant women at all trimesters showed no difference from those in nonpregnant women at any stage of the menstrual cycle. Recombinant sIL-6R (rsIL-6R) augmented hCG production by rIL-6-stimulated trophoblasts dose dependently, but failed to enhance hCG production by unstimulated trophoblasts. rIL-6- and rsIL-6R-induced hCG production was significantly blocked by anti-IL-6R antibody, PM1; antisignal transducing glycoprotein 130 (gp130) antibody, GPX7; or a tyrosine kinase inhibitor, genistein. Thus, sIL-6R in serum from pregnant women forms a complex with placental and decidual IL-6 in a manner similar to trophoblast membrane-bound IL-6R. These two discrete types of IL-6R and IL-6 complex might act cooperatively by binding to gp130 and subsequently evoking tyrosine kinase activity in the trophoblasts to produce hCG in vivo.

CT EMTAGS: pregnancy (0030); immunological procedures (0102); cytology (0332); mammal (0738); human (0888); female (0042); human tissue, cells or cell components (0111); priority journal (0007); article (0060); enzyme (0990)
Medical Descriptors:
*signal transduction
*interleukin receptor
third trimester pregnancy
menstrual cycle
enzyme inhibition

hormone synthesis
trophoblast
immunocytochemistry
hormone determination
statistical analysis
human
female
human tissue
human cell
priority journal
article
Drug Descriptors:
*interleukin 6: EC, endogenous compound
*chorionic gonadotropin: EC, endogenous compound
genistein: PD, pharmacology
protein tyrosine kinase

L109 ANSWER 13 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95272887 EMBASE Bioavailability of soybean isoflavones depends upon gut microflora in women. Xu X.; Harris K.S.; Wang H.-J.; Murphy P.A.; Hendrich S.. Food Science and Human Nutrition, Iowa State University, Ames, IA 50011, United States. Journal of Nutrition 125/9 (2307-2315) 1995. ISSN: 0022-3166. CODEN: JONUAI. Pub. Country: United States. Language: English. Summary Language: English.

AB Soybean isoflavones have been proposed to be anticarcinogenic, but their effective doses have not been established. To study their bioavailability, seven women consumed 3.4, 6.9, or 10.3 .mu.mol isoflavones/kg body wt in soymilk in each of three meals of a liquid diet on one of three feeding days that were separated by 2-wk washout periods. Subjects were randomly assigned to doses in a cross-over design. Plasma, urine and fecal isoflavones were measured by reverse phase HPLC. In two subjects, fecal isoflavone recovery was 10-20 times that in the other five subjects. Average 48-h urinary recoveries of ingested daidzein and genistein were 16 .+-. 4 and 10 .+-. 4%, respectively, at all three doses among the five subjects excreting only small amounts of isoflavones in feces, whereas urinary recoveries of daidzein and genistein in the two subjects who excreted large amounts of fecal isoflavones were 32 .+-. 5 and 37 .+-. 6%, respectively. Urinary isoflavone excretion was nearly zero in all subjects at 48 h after dosing. Average plasma concentration of genistein at 24 h after the breakfast isoflavone dose in subjects excreting large amounts of fecal isoflavones was significantly greater by 2.5-fold than in subjects who excreted small amounts of fecal isoflavones ($P < 0.05$). In vitro anaerobic incubation of isoflavones with human feces showed that intestinal half-life of daidzein and genistein may be as little as 7.5 and 3.3 h, respectively. These data suggest that human isoflavone bioavailability depends upon the relative ability of gut microflora to degrade these compounds.

CT EMTAGS: pharmacokinetics (0194); higher plant (0697); plant (0699); microorganism (0724); mammal (0738); human (0888); female (0042); human experiment (0104); normal human (0800); adult (0018); article (0060)
Medical Descriptors:
*drug bioavailability
*gastrointestinal absorption
*antineoplastic activity
***soybean**
milk
dietary intake
drug blood level
drug urine level
drug feces level
intestine flora
biodegradation
urinary excretion
reversed phase high performance liquid chromatography
human

female
human experiment
normal human
adult
article
Drug Descriptors:
*isoflavone: CR, drug concentration
*isoflavone: DO, drug dose
*isoflavone: PK, pharmacokinetics
*isoflavone: PD, pharmacology
***genistein: CR, drug concentration**
***genistein: DO, drug dose**
***genistein: PK, pharmacokinetics**
***genistein: PD, pharmacology**
***daidzein: CR, drug concentration**
***daidzein: DO, drug dose**
***daidzein: PK, pharmacokinetics**
***daidzein: PD, pharmacology**

L109 ANSWER 14 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
96070974 EMBASE Metabolism of daidzein and genistein by intestinal bacteria. Chang Y.-C.; Nair M.G.. Department of Horticulture, Pesticide Research Center, Michigan State University, East Lansing, MI 48824, United States. Journal of Natural Products 58/12 (1892-1896) 1995. ISSN: 0163-3864. CODEN: JNPRDF. Pub. Country: United States. Language: English. Summary Language: English.
AB The isoflavones daidzen [1] and genistein [2] were fermented with human fecal bacteria under anaerobic conditions. Dihydrodaidzen [3], benzopyran- 4,7-diol, 3-(4-hydroxyphenyl) [4], and equol [5] were isolated from the fermentation broth of 1. Only one metabolite, dihydrogenistein [6], was isolated and characterized from the fermentation broth of 2. Metabolites 3-6 were identified by spectral methods.
CT EMTAGS: microorganism (0724); pharmacokinetics (0194); higher plant (0697); plant (0699); nonhuman (0777); article (0060)
Medical Descriptors:
*drug isolation
***breast cancer**
intestine flora
drug metabolism
feces microflora
fermentation
soybean
antineoplastic activity
nonhuman
article
Drug Descriptors:
*isoflavone derivative: DV, drug development
***daidzein: DV, drug development**
***genistein: DV, drug development**
dihydrodiadzein: DV, drug development
benzopyran 4,7 diol,3 (4 hydroxyphenyl): DV, drug development
dihydrogenistein: DV, drug development
unclassified drug

L109 ANSWER 15 OF 79 MEDLINE
95382551 Structural requirements for differentiation-induction and growth-inhibition of mouse erythroleukemia cells by isoflavones. Jing Y; Waxman S. (Department of Medicine, Mount Sinai School of Medicine, New York, NY 10029, USA..)ANTICANCER RESEARCH, (1995 Jul-Aug) 15 (4) 1147-52. Journal code: 59L. ISSN: 0250-7005. Pub. country: Greece. Language: English.
AB Isoflavones are natural plant phytoestrogens which have been shown to have anticancer proliferation, differentiation and chemopreventive effects. In order to determine structure-function requirements, we compared the effects of several isoflavone derivatives and one flavone on mouse erythroleukemia (MEL) cell growth and differentiation. All chemicals tested are closely related in structure to genistein (4',5,7-trihydroxyisoflavone), a known

differentiation inducer and tyrosine protein kinase inhibitor. Genistein, daidzein (4',7-dihydroxyisoflavone) and genistin (7-glucoside of genistein) induced differentiation of MEL cells based on benzidine staining. Biochanin A (5,7-dihydroxy-4'-methoxyisoflavone) and apigenin (4',5,7-trihydroxyflavone) had no differentiation inducing effect. The potency of these chemicals on cell growth inhibition was apigenin > genistein > genistin > biochanin A > daidzein. These results suggest that the isoflavone structure and 4'-hydroxyl group are essential for the differentiation induction effect, whereas trihydroxyl derivatives are good growth inhibitors. Daidzein is a potent differentiation inducer with the least cytotoxic effect.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Antineoplastic Agents, Phytogenic: PD, pharmacology
Cell Differentiation: DE, drug effects
Cell Division: DE, drug effects
DNA Damage
Flavones: PD, pharmacology
*Isoflavones: PD, pharmacology
Leukemia, Erythroblastic, Acute: PA, pathology
Mice
Oils, Volatile: PD, pharmacology
Structure-Activity Relationship
Tumor Cells, Cultured

L109 ANSWER 16 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95087771 EMBASE Insulin stimulates endothelin-1 secretion from human endothelial cells and modulates its circulating levels in vivo. Ferri C.; Pittoni V.; Piccoli A.; Laurenti O.; Cassone M.R.; Bellini C.; Properzi G.; Valesini G.; De Mattia G.; Santucci A.. Fondazione Andrea Cesalpino, Istituto di I Clinica Medica, Universita 'La Sapienza', 00161 Rome, Italy. Journal of Clinical Endocrinology and Metabolism 80/3 (829-835) 1995. ISSN: 0021-972X. CODEN: JCEMAZ. Pub. Country: United States. Language: English. Summary Language: English.

AB Endothelin-1 (ET-1) is a potent vasoactive and mitogenic peptide produced by the vascular endothelium. In this study, we evaluated whether insulin stimulates ET-1 secretion by human endothelial cells derived from umbilical cord veins and by human permanent endothelial hybrid cells Ea.hy 926. Moreover, to provide evidence that insulin may stimulate ET-1 secretion in vivo, plasma ET-1 levels were evaluated in 7 type II diabetic normotensive males (mean age, 54.3 .+-. 4.0 yr) during 2-h hyperinsulinemic euglycemic clamps (287 pmol insulin/m2 .cntdot. min-1) as well as in 12 obese hypertensive males (mean age, 44.2 .+-. 4.6 yr) before and after a 12-week period of caloric restriction. Our results showed that insulin stimulated ET-1 release from cultured endothelial cells in a dose-dependent fashion. ET-1 release persisted for 24 h and was also observed at physiological insulin concentrations (10-9 mol/L). The insulin-induced ET-1 secretion was inhibited by genistein, a tyrosine kinase inhibitor, and by cycloheximide, a protein synthesis inhibitor, suggesting that it requires de novo protein synthesis rather than ET-1 release from intracellular stores. In the in vivo experiments, plasma ET-1 levels rapidly increased during euglycemic hyperinsulinemic clamps (from 0.76 .+-. 0.18 pg/mL at time zero to 1.65 .+-. 0.21 pg/mL at 60 min; $P < 0.05$) and persisted elevated until the end of insulin infusion (1.37 .+-. 0.37 pg/mL at 120 min; $P < 0.05$ vs. time zero). In obese hypertensives, plasma ET-1 levels significantly decreased after 12 weeks of caloric restriction (from 0.85 .+-. 0.51 to 0.48 .+-. 0.28 pg/mL; $P < 0.04$). The decrease in body weight induced by caloric restriction was accompanied by a significant reduction in fasting insulin levels (from 167.2 .+-. 94.0 to 98.9 .+-. 44.9 pmol/L; $P < 0.05$) which correlated with the reduction in plasma ET-1 levels ($r = 0.78$; $P < 0.003$). In conclusion, our data show that insulin stimulates both in vitro and in vivo ET-1 secretion. Such interaction could play a significant role in the development of atherosclerotic lesions in hyperinsulinemic conditions.

CT EMTAGS: therapy (0160); diagnosis (0140); genetic engineering and gene technology (0108); heredity (0137); mammal (0738); human (0888); male (0041); clinical article (0152); controlled study (0197); human tissue, cells or cell components (0111); adult (0018); priority journal (0007); article (0060)
Medical Descriptors:
*insulin treatment
*diabetes mellitus
*essential hypertension
*hyperinsulinemia
obesity
dose response
endothelium cell
high performance liquid chromatography
caloric restriction
weight reduction
protein synthesis
glucose clamp technique
hybrid cell
human
male
clinical article
clinical trial
controlled study
human cell
adult
priority journal
article
Drug Descriptors:
*insulin: CT, clinical trial
*insulin: CB, drug combination
*insulin: DO, drug dose
*insulin: PD, pharmacology
***genistein: CB, drug combination**
***genistein: PD, pharmacology**
*cycloheximide: CB, drug combination
*cycloheximide: PD, pharmacology
*dactinomycin: CB, drug combination
*dactinomycin: PD, pharmacology
*somatomedin c: PD, pharmacology
*endothelin 1: EC, endogenous compound
enzyme inhibitor: CB, drug combination
enzyme inhibitor: PD, pharmacology
protein synthesis inhibitor: CB, drug combination
protein synthesis inhibitor: PD, pharmacology
glucose: PD, pharmacology
cholesterol: EC, endogenous compound
triacylglycerol: EC, endogenous compound
unclassified drug
protein tyrosine kinase inhibitor: CB, drug combination
protein tyrosine kinase inhibitor: PD, pharmacology

L109 ANSWER 17 OF 79 MEDLINE
95190660 Genistein, a dietary ingested isoflavonoid, inhibits cell proliferation and in vitro angiogenesis. Fotsis T; Pepper M; Adlercreutz H; Hase T; Montesano R; Schweigerer L. (Department of Oncology and Immunology, Children's University Hospital, Ruprecht-Karls Universitat, Heidelberg, Germany..)JOURNAL OF NUTRITION, (1995 Mar) 125 (3 Suppl) 790S-797S. Ref: 45. Journal code: JEV. ISSN: 0022-3166. Pub. country: United States. Language: English.
AB Consumption of a plant-based diet can prevent the development and progression of chronic diseases that are associated with extensive neovascularization. To determine whether prevention might be associated with dietary derived angiogenesis inhibitors, we have fractionated urine of healthy human subjects consuming a plant-based diet and examined the fractions for their abilities to inhibit the proliferation of vascular endothelial cells. One of the most potent fractions contained several isoflavonoids, which we identified by

gas chromatography-mass spectrometry and subsequently synthesized. Of all synthetic compounds, the isoflavonoid genistein was the most potent and inhibited endothelial cell proliferation and in vitro angiogenesis at half maximal concentrations of 5 and 150 mumol/L, respectively. Moreover, genistein inhibited the proliferation of various tumor cells. Genistein excretion in urine of subjects consuming a plant-based diet is in the micromolar range, which is 30-fold higher than that of subjects consuming a traditional Western diet. The high concentrations of genistein in urine of vegetarians and our present results suggest that genistein may contribute to the preventive effect of plant-based diet on chronic diseases, including solid tumors, by inhibiting neovascularization and tumor cell proliferation. Thus genistein may have important applications in the treatment of solid tumors and angiogenic diseases.

CT Check Tags: Animal; Human; Male; Support, Non-U.S. Gov't
*Antineoplastic Agents: PD, pharmacology
Cell Division: DE, drug effects
***Cell Transformation, Neoplastic: DE, drug effects**
Diet
*Isoflavones: PD, pharmacology
***Neoplasms: PA, pathology**
Neoplasms, Experimental: PA, pathology
*Neovascularization, Pathologic: PC, prevention & control
Rats

L109 ANSWER 18 OF 79 MEDLINE
95190658 Effect of genistein on in vitro and in vivo models of cancer. Barnes S. (Department of Pharmacology, University of Alabama at Birmingham 35294..)JOURNAL OF NUTRITION, (1995 Mar) 125 (3 Suppl) 777S-783S. Ref: 61. Journal code: JEV. ISSN: 0022-3166. Pub. country: United States. Language: English.

AB In two-thirds of studies on the effect of genistein-containing soy materials in animal models of cancer, the risk of cancer (incidence, latency or tumor number) was significantly reduced. In addition, purified genistein delayed mammary tumor appearance in association with increased cell differentiation in mammary tissue in rats treated with 7, 12-dimethylbenz[a]anthracene when administered neonatally, inhibited phorbol ester-induced H2O2 production in a model of skin cancer, and inhibited aberrant crypt formation in a model of colonic cancer. In in vitro models, genistein inhibited the proliferation of human tumor cell lines in culture with a wide variation in IC50 values (2.6-79 mumol/L, or 1-30 micrograms/mL). In only a few cases was the IC50 below 13.2 mumol/L (5 micrograms/mL), the presumed upper limit for the serum genistein concentration in those on a high soy diet. In future studies, greater emphasis should be placed on the effect of genistein on nontransformed, normal cell lines from the tissues where cancer can occur rather than established tumor cell lines. Similarly, the effect of genistein on the progression and/or promotion of cancer may be more clearly examined using nontransformed cell lines transfected with specific oncogenes thought to be activated during oncogenesis.

CT Check Tags: Animal; Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Antineoplastic Agents: TU, therapeutic use
Breast Neoplasms: DH, diet therapy
Breast Neoplasms: EP, epidemiology
Breast Neoplasms: PA, pathology
***Colonic Neoplasms: DH, diet therapy**
Colonic Neoplasms: DT, drug therapy
Colonic Neoplasms: EP, epidemiology
Disease Models, Animal
Incidence
Isoflavones: AN, analysis
*Isoflavones: TU, therapeutic use
***Mammary Neoplasms, Experimental: DH, diet therapy**
Mammary Neoplasms, Experimental: DT, drug therapy
Mammary Neoplasms, Experimental: EP, epidemiology
Mice
Prostatic Neoplasms: DH, diet therapy

Prostatic Neoplasms: EP, epidemiology
Prostatic Neoplasms: PA, pathology
Rats
Risk Factors
***Skin Neoplasms: DH, diet therapy**
Skin Neoplasms: DT, drug therapy
Skin Neoplasms: EP, epidemiology
***Soybeans**
Soybeans: CH, chemistry
Tumor Cells, Cultured

L109 ANSWER 19 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95074008 EMBASE Soybean phytoestrogen intake and cancer risk. Herman C.; Adlercreutz T.; Goldin B.R.; Gorbach S.L.; Hockerstedt K.A.V.; Watanabe S.; Hamalainen E.K.; Markkanen M.H.; Makela T.H.; Wahala K.T.; Hase T.A.; Fotsis T.. Department of Clinical Chemistry, University of Helsinki, Meilahti Hospital, FIN-00290 Helsinki, Finland. Journal of Nutrition 125/3 SUPPL. (757S-770S) 1995. ISSN: 0022-3166. CODEN: JONUAI. Pub. Country: United States. Language: English. Summary Language: English.

AB Because many Western diseases are hormone-dependent cancers, we have postulated that the Western diet, compared with a vegetarian or semivegetarian diet, may alter hormone production, metabolism or action at the cellular level. Recently, our interest has been focused on the cancer- protective role of some hormone-like diphenolic phytoestrogens of dietary origin, the lignans and isoflavonoids. The precursors of the biologically active compounds originate in soybean products (mainly isoflavonoids but also lignans), as well as whole grain cereals, seeds, probably berries and nuts (mainly lignans). The plant lignan and isoflavonoid glycosides are converted by intestinal bacteria to hormone-like compounds with weak estrogenic and antioxidative activity; they have now been shown to influence not only sex hormone metabolism and biological activity but also intracellular enzymes, protein synthesis, growth factor action, malignant cell proliferation, differentiation and angiogenesis, making them strong candidates for a role as natural cancer protective compounds. Epidemiological investigations support this hypothesis, because the highest levels of these compounds are found in countries or regions with low cancer incidence. This report is a review of results that suggest that the diphenolic isoflavonoids and lignans are natural cancer-protective compounds.

CT EMTAGS: **malignant neoplastic disease** (0306); epidemiology (0400); prevention (0165); therapy (0160); higher plant (0697); plant (0699); mammal (0738); human (0888); nonhuman (0777); conference paper (0061); enzyme (0990)
Medical Descriptors:
***cancer: EP, epidemiology**
***cancer: PC, prevention**
***cancer: TH, therapy**
cancer risk
soybean
diet
estrogen activity
antioxidant activity
cancer prevention
estrogen binding
enzyme inhibition
breast cancer: EP, epidemiology
breast cancer: PC, prevention
colorectal cancer: EP, epidemiology
colorectal cancer: PC, prevention
human
nonhuman
conference paper
Drug Descriptors:
*estrogen derivative: PD, pharmacology
*lignan: PD, pharmacology
*isoflavone: PD, pharmacology

enterolactone: PD, pharmacology
daidzein: PD, pharmacology
aromatase
sex hormone binding globulin
protein tyrosine kinase
growth factor

L109 ANSWER 20 OF 79 MEDLINE
95190655 In vitro hormonal effects of soybean isoflavones. Molteni A; Brizio-Molteni L; Persky V. (Department of Pathology, Northwestern University, Chicago, IL..)JOURNAL OF NUTRITION, (1995 Mar) 125 (3 Suppl) 751S-756S. Ref: 30. Journal code: JEV. ISSN: 0022-3166. Pub. country: United States. Language: English.
AB Isoflavones exhibit a multitude of biological effects that influence cell growth and regulation, and, thus, may have potential value in the prevention and treatment of cancer. Isoflavones are weak estrogens and can function both as estrogen agonists and antagonists depending on the hormonal milieu and the target tissue and species under investigation. Genistein, one of the two primary isoflavones in soybeans, has attracted much attention from the research community, not only because of its potential antiestrogenic effects, but because it inhibits several key enzymes thought to be involved in carcinogenesis. Although still speculative, greater dietary incorporation of soybean products, because of the high concentration of isoflavones, may be a safe and effective means of reducing cancer risk.
CT Check Tags: Animal; Human
Antineoplastic Agents: ME, metabolism
Antineoplastic Agents: PD, pharmacology
Antineoplastic Agents: TU, therapeutic use
Estrogen Antagonists: ME, metabolism
*Estrogen Antagonists: PD, pharmacology
Estrogen Antagonists: TU, therapeutic use
*Estrogens: AG, agonists
Estrogens: ME, metabolism
Growth Substances: ME, metabolism
Growth Substances: PD, pharmacology
Growth Substances: TU, therapeutic use
Isoflavones: ME, metabolism
*Isoflavones: PD, pharmacology
Isoflavones: TU, therapeutic use
Neoplasms: DH, diet therapy
Neoplasms: PC, prevention & control
Neoplasms, Experimental: DH, diet therapy
Neoplasms, Experimental: PC, prevention & control
Protein Binding
*Receptors, Estrogen: ME, metabolism
***Soybeans**
Soybeans: CH, chemistry

L109 ANSWER 21 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95309399 EMBASE Screening of phagocyte activators in plants; enhancement of TNF production by flavonoids. Kunizane H.; Ueda H.; Yamazaki M.. Faculty of Pharmaceutical Sciences, Department of Medicinal Chemistry, Teikyo University, 1091-1 Suarashi, Sagamiko-machi, Tsukui-gun, Kanagawa 199-01, Japan. Yakugaku Zasshi 115/9 (749-755) 1995. ISSN: 0031-6903. CODEN: YKKZAJ. Pub. Country: Japan. Language: Japanese. Summary Language: English; Japanese.
AB The tumor necrosis factor (TNF) was first discovered as a substance that induced necrosis of transplanted tumors. Recently, TNF has been recognized as an important and endogenous mediator in host defense mechanisms. To prove the fact that plant foods contain substances which activate the host defense mechanisms, we first examined if the administration of flavonoids could induce TNF production in mice. Some selected flavonoids such as naringin, apiin, poncirin and rutin were shown to amplify TNF release from murine macrophages in vivo in response to OK-432 as a second stimulus. However, their aglycone forms were not effective. The differences in the saccharide- chain of flavonoids induced the variety of TNF production.

CT EMTAGS: reticuloendothelial system (0924); plant (0699); nonhuman (0777); mouse (0727); mammal (0738); animal experiment (0112); controlled study (0197); animal tissue, cells or cell components (0105); intravenous drug administration (0182); article (0060)
Medical Descriptors:
***tumor necrosis**
*host resistance
macrophage
plant
food composition
dose response
nonhuman
mouse
animal experiment
controlled study
animal cell
intravenous drug administration
article
Drug Descriptors:
*tumor necrosis factor: EC, endogenous compound
*flavonoid: AD, drug administration
*flavonoid: DV, drug development
*flavonoid: DO, drug dose
*aurantiin: AD, drug administration
*aurantiin: DV, drug development
*aurantiin: DO, drug dose
*apiin: AD, drug administration
*apiin: DV, drug development
*apiin: DO, drug dose
*rutoside: AD, drug administration
*rutoside: DV, drug development
*rutoside: DO, drug dose
*picibanil: AD, drug administration
*picibanil: DV, drug development
*picibanil: DO, drug dose
apigenin
daidzein
genistein
hesperidin
quercetin
phloretin
phlorizin
puerarin
poncirin: AD, drug administration
poncirin: DV, drug development
poncirin: DO, drug dose
unclassified drug

L109 ANSWER 22 OF 79 MEDLINE DUPLICATE 1
95190653 The evidence for soybean products as cancer preventive agents. Kennedy A R. (Department of Radiation Oncology, University of Pennsylvania School of Medicine, Philadelphia 19104..)JOURNAL OF NUTRITION, (1995 Mar) 125 (3 Suppl) 733S-743S. Ref: 92. Journal code: JEV. ISSN: 0022-3166. Pub. country: United States. Language: English.
AB There is much evidence suggesting that compounds present in soybeans can prevent cancer in many different organ systems. The evidence for specific soybean-derived compounds having a suppressive effect on carcinogenesis in animal model systems is limited, however. There is evidence that the following isolated soybean derived products suppress carcinogenesis in vivo: a protease inhibitor, the Bowman-Birk inhibitor, inositol hexaphosphate (phytic acid) and the sterol beta-sitosterol. Other compounds that may be able to suppress carcinogenesis in animals are the soybean isoflavones. Soybean compounds reported to have other types of anticarcinogenic activity include soybean trypsin inhibitor, saponins and genistein. There is much evidence to suggest that diets containing large amounts of soybean products are associated with overall low cancer mortality rates, particularly for cancers of the colon, breast and prostate.

It is believed that supplementation of human diets with certain soybean products shown to suppress carcinogenesis in animals could markedly reduce human cancer mortality rates.

CT Check Tags: Animal; Human; Support, U.S. Gov't, P.H.S.
Antineoplastic Agents: AE, adverse effects
*Antineoplastic Agents: ST, standards
Antineoplastic Agents: TU, therapeutic use
Dietary Proteins: AE, adverse effects
Dietary Proteins: ST, standards
Dietary Proteins: TU, therapeutic use
Disease Models, Animal
Hamsters
Isoflavones: AE, adverse effects
Isoflavones: ST, standards
Isoflavones: TU, therapeutic use
Mice
Neoplasms: DH, diet therapy
***Neoplasms: PC, prevention & control**
Neoplasms, Experimental: DH, diet therapy
***Neoplasms, Experimental: PC, prevention & control**
Protease Inhibitors: AE, adverse effects
Protease Inhibitors: ST, standards
Protease Inhibitors: TU, therapeutic use
Rats
Saponins: AE, adverse effects
Saponins: ST, standards
Saponins: TU, therapeutic use
***Soybeans**
Soybeans: CH, chemistry
Vegetable Proteins: AE, adverse effects
*Vegetable Proteins: ST, standards
Vegetable Proteins: TU, therapeutic use

L109 ANSWER 23 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95310828 EMBASE Genetic and cellular changes in colorectal cancer: Proposed targets of chemopreventive agents. Greenwald P.; Kelloff G.J.; Boone C.W.; McDonald S.S.. Cancer Prevention/Control Division, National Cancer Institute, Building 31, 9000 Rockville Pike, Bethesda, MD 20892, United States. Cancer Epidemiology Biomarkers and Prevention 4/7 (691-702) 1995. ISSN: 1055-9965. CODEN: CEBPE4. Pub. Country: United States. Language: English. Summary Language: English.

AB Progress in development of a genetic model for colorectal tumorigenesis and human chemoprevention research may allow the mechanism-based identification of targets and chemopreventive agents that will protect against colorectal cancer. For example, numerous mutagenic events can occur throughout colorectal carcinogenesis, including loss of heterozygosity in tumor suppressor genes such as APC, MCC, DCC, and p53, as well as in oncogenes such as K-ras. Chemopreventive agents that inhibit mutagenic activity such as N-acetyl-l-cysteine, oltipraz, and nonsteroidal anti- inflammatory drugs may protect against these mutations. Also, agents such as perillyl alcohol and lovastatin that interfere with protein isoprenylation and, hence, inhibit oncogene activation may protect against aberrant K-ras expression. Hyperproliferation in normal mucosa, leading to early adenomas, and cellular proliferation, leading to growth and progression of neoplasia, are also aspects of colorectal carcinogenesis that can be controlled by chemopreventive agents. Calcium is a chemopreventive agent for which there is both clinical and experimental evidence of inhibition of cell proliferation in colon mucosa. Other examples of antiproliferative agents with potential chemopreventive efficacy in colon are 2-difluoromethylornithine, dehydroepiandrosterone, and selenium. Differentiating agents such as retinoids and deltanoids also may slow proliferation and progression. Antioxidants have potential for interfering with both mutagenicity and proliferation (e.g., by preventing oxidative activation of carcinogens and scavenging activated oxygen species generated during inflammation). The same mechanistic principles apply to identification of dietary

chemopreventive intervention for colorectal carcinogenesis. For example, lowering dietary fat and increasing dietary fiber lead to lower colorectal mucosal proliferation, and cruciferous vegetables contain agents such as indoles and dithiolthiones that have shown antimutagenic activity.

CT EMTAGS: epidemiology (0400); etiology (0135); prevention (0165); therapy (0160); malignant neoplastic disease (0306); mammal (0738); human (0888); nonhuman (0777); mouse (0727); rat (0733); animal model (0106); biological model (0502); priority journal (0007); article (0060)

Medical Descriptors:
*colorectal cancer: EP, epidemiology
*colorectal cancer: ET, etiology
*colorectal cancer: PC, prevention
colon carcinogenesis
cancer model
cancer risk
dietary intake
cancer prevention
antioxidant activity
drug effect
cancer growth
tumor suppressor gene
human
nonhuman
mouse
rat
clinical trial
phase 2 clinical trial
animal model
priority journal
article

Drug Descriptors:
*acetylcysteine: PD, pharmacology
*oltipraz: PD, pharmacology
*nonsteroid antiinflammatory agent: PD, pharmacology
*mevinolin: PD, pharmacology
*calcium: CT, clinical trial
*calcium: PD, pharmacology
prasterone: PD, pharmacology
eflornithine: PD, pharmacology
selenium: PD, pharmacology
antioxidant: PD, pharmacology
polyphenol: PD, pharmacology
alpha tocopherol: PD, pharmacology
curcumin: PD, pharmacology
fumaric acid: PD, pharmacology
genistein: PD, pharmacology
quercetin: PD, pharmacology
limonene: PD, pharmacology
retinoid: PD, pharmacology
vitamin d derivative: PD, pharmacology
terpene: PD, pharmacology
flavonoid: PD, pharmacology
isothiocyanic acid: PD, pharmacology
ellagic acid: PD, pharmacology
sulindac: PD, pharmacology
indometacin: PD, pharmacology
ibuprofen: PD, pharmacology
piroxicam: PD, pharmacology
folic acid: PD, pharmacology
acetylsalicylic acid: PD, pharmacology
heterocyclic amine: TO, drug toxicity
unindexed drug

L109 ANSWER 24 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95220568 EMBASE Effect of diet on lignans and isoflavonoid phytoestrogens in chimpanzees. Musey P.I.; Adlecreutz H.; Gould K.G.; Collins D.C.; Fotsis T.; Bannwart C.; Makela T.; Wahala K.;

Brunow G.; Hase T.. Department Biological Sciences, Clark Atlanta University, Atlanta, GA 30314, United States. Life Sciences 57/7 (655-664) 1995. ISSN: 0024-3205. CODEN: LIFSAK. Pub. Country: United States. Language: English. Summary Language: English.

AB Diphenolic compounds belonging to the class of lignans and isoflavonoids have been identified in urine or man and animals, including the chimpanzee. Some of these compounds, formed by intestinal bacteria from plant ligans and phytoestrogens, have been shown in animal studies to exhibit biological activities that suggest they could function as cancer-protective compounds. The effect of diet on urinary excretion of these compounds in the adult male chimpanzee has been studied. It was found that the chimpanzee consuming their regular food excreted large amounts of the isovlavonoid phytoestrogens, equol (mean .+-. SE) (127.5 .+-. 34.0 nmol/mg cr.) and daidzein (20.7 .+-. 9.0 nmol/mg cr.) and the lignan, enterolactone (14.1 .+-. 3.5 nmol/mg cr.). Small amounts of the lignan, enterodiol, (0.4 .+-. 0.2 nmol/mg cr.) were also excreted. On all other four test diets (high protein, high carbohydrate, high vegetable, and high fat), the excretion was less, particularly on a high fat diet where the excretion of all diphenolic compounds was reduced by more than 90% to a level observed in omnivorous human subjects or women with breast cancer. These results suggest that diet profoundly influences the excretion of both animal lignans and phytoestrogens in urine. Because non-human primates are particularly resistant to mammary and genital carcinoma on estrogen treatment, the present data suggest that the very high levels of phytoestrogens and lignans as found during exposure to the regular diet may partially account for why these primates are so resistant to hormonal manipulations to induce cancer.

CT EMTAGS: therapy (0160); prevention (0165); ape (0726); mammal (0738); higher plant (0697); plant (0699); **malignant neoplastic disease** (0306); nonhuman (0777); controlled study (0197); animal experiment (0112); male (0041); article (0060)
Medical Descriptors:
*cancer prevention
***diet**
chimpanzee
vegetable
breast carcinoma
genital tract cancer
urinary excretion
protein diet
carbohydrate diet
lipid diet
nonhuman
controlled study
animal experiment
male
article
Drug Descriptors:
*lignan
*isoflavonoid
*estrogen
daidzein
enterolactone
unclassified drug
phytoestrogen
equol
enterodiol

L109 ANSWER 25 OF 79 MEDLINE
95314632 Potent inhibition of breast cancer cell lines by the isoflavonoid kievitone: comparison with genistein. Hoffman R. (Clinical Oncology and Radiotherapeutics Unit, MRC Centre, Cambridge, UK..)BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1995 Jun 15) 211 (2) 600-6. Journal code: 9Y8. ISSN: 0006-291X. Pub. country: United States. Language: English.

AB The isoflavonoid kievitone potently inhibited the proliferation of

the oestrogen receptor (ER)-positive breast cancer cell lines MCF-7 and T47D and the ER-negative breast cancer cell line SKBR3 (IC50 values 5-18 microM). DNA synthesis of MCF-7 cells stimulated by insulin-like growth factor 1, insulin-like growth factor 2, basic fibroblast growth factor or transforming growth factor alpha was inhibited by similar concentrations of kievitone (IC50 values 1-3 microM). DNA synthesis stimulated by 17, beta-oestradiol was also inhibited (IC50 = 6 microM). Compared with kievitone, genistein was 3-9 fold weaker as an inhibitor of the proliferation of the breast cancer cell lines and of growth factor-stimulated DNA synthesis. However, genistein was about 5-fold more potent than kievitone as an inhibitor of solubilised epidermal growth factor (EGF) receptor kinase activity and EGF receptor autophosphorylation.

CT Check Tags: Comparative Study; Human
*Antineoplastic Agents: PD, pharmacology
Breast Neoplasms
*Cell Division: DE, drug effects
Cell Line
Dose-Response Relationship, Drug
DNA Replication: DE, drug effects
Epidermal Growth Factor Receptor Protein-Tyrosine Kinase: AI, antagonists & inhibitors
Fibroblast Growth Factor, Basic: PD, pharmacology
Insulin-Like Growth Factor I: PD, pharmacology
Insulin-Like Growth Factor II: PD, pharmacology
Isoflavones: IP, isolation & purification
*Isoflavones: PD, pharmacology
Legumes
Molecular Structure
Phosphorylation
Receptors, Epidermal Growth Factor-Urogastrone: ME, metabolism
Receptors, Estrogen: AN, analysis
Tumor Cells, Cultured
Tumor Necrosis Factor: PD, pharmacology

L109 ANSWER 26 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95147272 EMBASE Urinary isoflavonoid phytoestrogen and lignan excretion after consumption of fermented and unfermented soy products. Hutchins A.M.; Slavin J.L.; Lampe J.W.. Division of Public Health Sciences, Fred Hutchinson Cancer Res. Center, 1124 Columbia St, Seattle, WA 98104, United States. Journal of the American Dietetic Association 95/5 (545-551) 1995. ISSN: 0002-8223. CODEN: JADAAE. Pub. Country: United States. Language: English. Summary Language: English.

AB Objective: To compare the effects of consumption of fermented and unfermented soy products on excretion of urinary isoflavonoid phytoestrogens and lignans in healthy men. Design: A randomized, crossover trial consisting of two 9-day feeding periods following 5 days of baseline data collection. Subjects: Healthy men, aged 20 to 40 years, were recruited from the University of Minnesota Twin Cities community. Of the 22 subjects who began the study, 17 completed all feeding periods. Interventions: Fermented soy product (112 g tempeh) or unfermented soy (125 g soybean pieces) was consumed during each controlled feeding period. Main outcome measure: Urine samples collected while subjects consumed their habitual diets and on the last 3 days of each feeding period were analyzed for isoflavonoid and lignan content by isotope dilution gas chromatography-mass spectrometry. Statistical analysis performed: Comparisons of isoflavonoid and lignan excretion were analyzed using the general linear model procedure. Orthogonal contrasts were used to determine treatment differences of interest. Results: Urinary excretion of isoflavonoids (equol, O-desmethylangolensin [O-DMA], daidzein, genistein) was higher and excretion of lignans (enterodiol, enterolactone) was lower when subjects consumed soy-supplemented diets than when they consumed their habitual diets ($P<.05$). Urinary isoflavonoid excretion anti lignan excretion were similar when subjects consumed tempeh and soybean pieces diets; however, recovery of daidzein and genistein was significantly higher when subjects consumed the tempeh diet than when they consumed the

soybean pieces diet (P<.002). When fed soy, 5 of 17 subjects excreted high amounts of equol. These five subjects tended to excrete less O-DMA and daidzein than the 12 subjects who excreted low amounts of equol (P<.06). Conclusions: Fermentation of soy decreased the isoflavone content of the product fed but increased the urinary isoflavonoid recovery. This finding suggests that fermentation increases availability of isoflavones in soy.

CT EMTAGS: higher plant (0697); plant (0699); therapy (0160); mammal (0738); human (0888); male (0041); human experiment (0104); normal human (0800); adult (0018); article (0060)
Medical Descriptors:
*soybean
*fermentation
*dietary intake
diet supplementation
urinalysis
urinary excretion
gas chromatography
mass spectrometry
crossover procedure
randomization
human
male
human experiment
normal human
adult
article
Drug Descriptors:
*isoflavonoid
*lignan
daidzein
genistein

L109 ANSWER 27 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95206165 EMBASE A simplified method to quantify isoflavones in commercial soybean diets and human urine after legume consumption.
Lu L.-J.W.; Broemeling L.D.; Marshall M.V.; Ramanujam V.M.S..
Prevent. Med./Community Health Dept., 2.102 Ewing Hall, University of Texas, 700 Strand, Galveston, TX 77555-1110, United States.
Cancer Epidemiology Biomarkers and Prevention 4/5 (497-503) 1995.
ISSN: 1055-9965. CODEN: CEBPE4. Pub. Country: United States.
Language: English. Summary Language: English.

AB Reliable and economical quantification of micronutrients in diets and humans is a critical component of successful epidemiological studies to establish relationships between dietary constituents and chronic disease. Legumes are one of the major dietary components consumed by populations worldwide. Consumption of legumes is thought to play a major role in lowering breast and prostate cancer risk. In this study, a simplified method that uses solid-phase extraction and gas chromatography was developed to measure isoflavones at levels down to 10 .mu.g/5 ml. With the use of this method, 12.5 g miso (a soybean paste), 12 ounces Isomil, and 12 ounces soymilk had daidzin/daidzein levels of 2, 5, and 12.4 mg, respectively, and genistin/genistein levels of 3, 6.5, and 13.7 mg, respectively. In these products, most of the isoflavones were present as glucosides. With the same method, urinary levels of isoflavones in six 15-17-year-old subjects were determined after soymilk ingestion. Each subject was placed on unrestricted nonsoya diets, and three 12-ounce portions of soymilk were given at 12-h intervals. Males excreted 15.02 .+-. 2.74 (SD) mg of daidzein glucuronides/sulfates [mean recovery, 40.4 .+-. 7.4% (SD)] by 24 h after the third soymilk ingestion, whereas females excreted 25.56 .+-. 5.10 mg (68.7 .+-. 13.7%) of daidzein conjugates, which was more than males (P = 0.02). Males and females excreted 7.73 .+-. 1.95 mg and 9.11 .+-. 0.84 mg of genistein glucuronides/sulfates (20% recovery of genistin intake), respectively, in the urine. Most of the isoflavones were excreted within 24 h after ingestion. The relative urinary levels of daidzein to genistein excreted were significantly (P < 0.05) higher in females than males after the third ingestion. The observed sex

difference requires more study since two of the females are siblings. Thus, the method described can be used to measure isoflavones in soya products and urinary excretion after soya ingestion.

CT EMTAGS: higher plant (0697); plant (0699); epidemiology (0400); etiology (0135); prevention (0165); mammal (0738); human (0888); male (0041); female (0042); human experiment (0104); normal human (0800); controlled study (0197); adolescent (0017); priority journal (0007); article (0060)

Medical Descriptors:
***soybean**
***legume**
***dietary intake**
*solid phase extraction
***breast cancer: EP, epidemiology**
***breast cancer: ET, etiology**
***breast cancer: PC, prevention**
***prostate cancer: EP, epidemiology**
***prostate cancer: ET, etiology**
***prostate cancer: PC, prevention**
urine level
urinary excretion
cancer risk
gas chromatography
human
male
female
human experiment
normal human
controlled study
adolescent
priority journal
article
Drug Descriptors:
*isoflavone
daidzein
genistein
glucoside
glucuronide

L109 ANSWER 28 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.

95029606 EMBASE Protein kinase C and tyrosine kinase pathways regulate lipopolysaccharide-induced nitric oxide synthase activity in RAW 264.7 murine macrophages. Paul A.; Pendreigh R.H.; Plevin R.. Dept. of Physiology/Pharmacology, University of Strathclyde, Royal College, 204 George Street, Glasgow G1 1XW, United Kingdom. British Journal of Pharmacology 114/2 (482-488) 1995. ISSN: 0007-1188. CODEN: BJPCBM. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB In RAW 264.7 macrophages, lipopolysaccharide (LPS) and .gamma.-interferon (IFN.gamma.) alone or in combination stimulated the induction of nitric oxide synthase (iNOS) activity and increased the expression of the 130 kDa isoform of NOS. LPS-induced NOS activity was reduced by incubation with CD14 neutralising antibodies and abolished in macrophages deprived of serum. LPS stimulated a small increase in protein kinase C (PKC) activity in RAW 264.7 macrophages which was dependent on the presence of serum. However, IFN.gamma. did not potentiate LPS-stimulated PKC activity. The protein kinase C inhibitor, Ro-318220, abolished both LPS- and IFN.gamma.-stimulated protein kinase C activity and the induction of NOS activity. LPS- and IFN.gamma.-induced NOS activity was reduced by the tyrosine kinase inhibitor genestein. Genestein also reduced LPS-stimulated protein kinase C activity but did not affect the response to the protein xinase C activator, tetradecanoylphorbol acetate (TPA). Nicotinamide, an inhibitor of poly-ADP ribosylation, abolished LPS- and IFN.gamma.-induced NOS activity. Brefeldin A, an inhibitor of a factor which stimulates nucleotide exchange activity on the 21 kDa ADP-ribosylation factor, ARF, reduced LPS- and IFN.gamma.-induced NOS activity by approximately 80%. These results

suggest the involvement of protein kinase C, tyrosine kinase and poly-ADP ribosylation pathways in the regulation of the induction of nitric oxide synthase in RAW 264.7 macrophages by LPS and IFN.gamma..

CT EMTAGS: reticuloendothelial system (0924); chemical procedures (0107); blood and hemopoietic system (0927); nonhuman (0777); mouse (0727); mammal (0738); controlled study (0197); animal tissue, cells or cell components (0105); priority journal (0007); article (0060); enzyme (0990); heredity (0137)
Medical Descriptors:
*macrophage
*enzyme regulation
protein phosphorylation
cell line
enzyme activity
drug antagonism
enzyme activation
enzyme induction
gene expression
serum
adenosine diphosphate ribosylation
nonhuman
mouse
controlled study
animal cell
priority journal
article
Drug Descriptors:
*lipopolysaccharide: TO, drug toxicity
*nitric oxide synthase: EC, endogenous compound
*protein kinase c: EC, endogenous compound
*protein tyrosine kinase: EC, endogenous compound
*gamma interferon: PD, pharmacology
*gamma interferon: IT, drug interaction
isoenzyme: EC, endogenous compound
ro 31 8220: PD, pharmacology
ro 31 8220: IT, drug interaction
protein kinase c inhibitor: PD, pharmacology
protein kinase c inhibitor: IT, drug interaction
phorbol 13 acetate 12 myristate: PD, pharmacology
nicotinamide: PD, pharmacology
nicotinamide: IT, drug interaction
brefeldin a: PD, pharmacology
brefeldin a: IT, drug interaction
neutralizing antibody
cd14 antigen: EC, endogenous compound
unclassified drug
genistein: PD, pharmacology
genistein: IT, drug interaction
protein tyrosine kinase inhibitor: PD, pharmacology
protein tyrosine kinase inhibitor: IT, drug interaction
protein kinase c activator: PD, pharmacology

L109 ANSWER 29 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95229103 EMBASE Comparative analysis of chemotaxis in dictyostelium using a radial bioassay method: Protein tyrosine kinase activity is required for chemotaxis to folate but not to cAMP. Browning D.D.; The T.; O'Day D.H.. Department of Zoology, Erindale College, University of Toronto, Mississauga, Ont. L5L 1C6, Canada. Cellular Signalling 7/5 (481-489) 1995. ISSN: 0898-6568. CODEN: CESIEY. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB The role of signal transduction during chemotaxis of Dictyostelium discoideum cells to cAMP and folic acid was investigated using a radial bioassay technique. The effects of signalling agonists were assessed by measuring the diameters of visible rings formed by the outward migration of amoebae up radial gradients of chemoattractant. This rapid and simple bioassay method yields chemotactic rates equivalent to more complex assay systems. In support of previous

studies, chemotaxis toward both cAMP and folic acid was inhibited in a dose-dependent manner by LaCl3, EDTA, chlorotetracycline and AlF3, supporting the importance of calcium ions and G protein-mediated signalling in both chemotactic events. The work was extended by examining the effects of the protein tyrosine kinase inhibitor genistein. This agent inhibited chemotaxis to folate in a dose-dependent manner but had no observable effect on chemotaxis toward cAMP. The notion that phosphorylation of proteins on tyrosine residues is critical for chemotaxis to folic acid was supported by Western blotting experiments with monoclonal anti-phosphotyrosine antibodies which detected two candidate proteins of M(r) 52,000 and 38,000 in the membranes of folate-responsive amoebae. These two bands disappeared with starvation which leads to the loss of responsiveness to folic acid and the acquisition of responsiveness to cAMP. Time-lapse videomicrography also revealed some unique differences in chemotactic response. Starved cells responded to cAMP as individuals but feeding cells chemoattracted to folic acid on a populational basis. The ability to compare two different types of chemotaxis using a simple, rapid and accurate bioassay system should enhance future studies of chemotaxis in wild-type and mutant strains of D. discoideum.

CT EMTAGS: invertebrate (0723); protozoon (0751); chemical procedures (0107); immunological procedures (0102); nonhuman (0777); controlled study (0197); priority journal (0007); article (0060); enzyme (0990)
Medical Descriptors:
*chemotaxis
signal transduction
sarcodina
bioassay
dictyostelium discoideum
cell migration
dose response
protein phosphorylation
immunoblotting
nonhuman
controlled study
priority journal
article
Drug Descriptors:
*protein tyrosine kinase: EC, endogenous compound
***folic acid: EC, endogenous compound**
*cyclic amp: EC, endogenous compound
chemoattractant: EC, endogenous compound
calcium ion: EC, endogenous compound
guanine nucleotide binding protein: EC, endogenous compound
lanthanum chloride
edetic acid
chlortetracycline
genistein: PD, pharmacology
membrane protein: EC, endogenous compound

L109 ANSWER 30 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95030619 EMBASE Regulation of apoptosis induced by the retinoid N-(4-hydroxyphenyl) retinamide and effect of deregulated bcl-2. Delia D.; Aiello A.; Formelli F.; Fontanella E.; Costa A.; Miyashita T.; Reed J.C.; Pierotti M.A.. Division of Experimental Oncology A, Istituto Nazionale Tumori, Via Venezian I, 20133 Milan, Italy. Blood 85/2 (359-367) 1995. ISSN: 0006-4971. CODEN: BLOOAW. Pub. Country: United States. Language: English. Summary Language: English.

AB The cancer chemopreventive retinoid N-(4-hydroxyphenyl)-all-trans retinamide (HPR) was recently shown by us to have antiproliferative and apoptotic effects on human leukemic cell lines, including those unresponsive to all-trans retinoic acid (ATRA). We have now characterized further the process of HPR-induced cell death. We report that inhibitors of RNA transcription and of protein synthesis, activators of protein kinase C (PKC), inhibitors of tyrosine kinases, Zn++, and the antioxidants acetylcysteine, ascorbic acid, alpha-tocopherol, and deferoxamine suppressed HPR-induced apoptosis. HL60 cells induced toward monocytic

differentiation by 1,25 dihydroxyvitamin-D3 [1,25(OH)2D3], but not those induced toward the granulocytic differentiation by ATRA, showed reduced responses to HPR. The transport of HPR by cells with different sensitivity to the retinoid, however, was similar, even after treatment with the phorbol ester 12-O- tetradecanoylphorbol-13-acetate (TPA), which induces unresponsiveness to HPR. The expression of the apoptosis-related genes bcl-2, p53, and c-myc was examined to determine their role in HPR-triggered cell death. The levels of bcl-2 mRNA were markedly diminished by 24 hours of HPR treatment in all cell lines except in the relatively HPR-insensitive line K422. However, probably because of its long half-life, bcl-2 protein levels were either unchanged or only slightly decreased. Downregulation of p53 mRNA was also observed within 24 hours of HPR exposure in NB4 but not K422 cells, but no changes in the amount of p53 protein were found. Suppression of c-myc transcription was observed in all cells except K422. The protective role of bcl-2 on cell death by HPR was investigated in HL60 as well as 697 pre-B leukemia and Jurkat T- acute lymphocytic leukemia (T-ALL) cells constitutively expressing high levels of bcl-2 proteins due to gene transfer manipulation. Compared with control cells, the onset of apoptosis in these cells with deregulated bcl-2 production was delayed by at least 24 hours. These findings establish that cell death by HPR requires RNA transcription and protein synthesis and is regulated by the activation of PKC. Although changes in bcl-2, p53, and c- myc expression are found in cells treated with HPR, the time-course of these events suggests that HPR-triggered apoptosis is not directly controlled by these genes. Finally, while ectopic overexpression of bcl-2 does not protect cells from death by HPR, it markedly delays its onset. This finding, together with the recently reported role of bcl-2 in an antioxidant pathway and with our evidence that antioxidants abrogate the effect of HPR, leads to the hypothesis that HPR may either induce apoptosis, at least in part, by eliciting oxidative stress or that oxidative stress accompanies apoptosis induced by HPR.

CT EMTAGS: heredity (0137); mammal (0738); human (0888); controlled study (0197); human tissue, cells or cell components (0111); priority journal (0007); article (0060)

Medical Descriptors:
*apoptosis
drug activity
drug effect
drug screening
cell strain hl 60
cell differentiation
gene expression
oncogene c myc
leukemia cell line
oxidative stress
human
controlled study
human cell
priority journal
article

Drug Descriptors:
***retinoid derivative: PD, pharmacology**
acetylcysteine: PD, pharmacology
ascorbic acid: PD, pharmacology
alpha tocopherol: PD, pharmacology
deferoxamine: PD, pharmacology
cycloheximide: PD, pharmacology
dactinomycin: PD, pharmacology
herbimycin: PD, pharmacology
genistein: PD, pharmacology
nicotinamide: PD, pharmacology
timonacic arginine: PD, pharmacology
zinc sulfate: PD, pharmacology
calcitriol: PD, pharmacology
retinoic acid: PD, pharmacology
aurintricarboxylic acid: PD, pharmacology

*fenretinide: PD, pharmacology

L109 ANSWER 31 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95180160 EMBASE Fecal lignan and isoflavonoid excretion in premenopausal women consuming flaxseed powder. Kurzer M.S.; Lampe J.W.; Martini M.C.; Adlercreutz H.. Department of Food Science/Nutrition, University of Minnesota, 1334 Eckles Avenue, St. Paul, MN 55108, United States. Cancer Epidemiology Biomarkers and Prevention 4/4 (353-358) 1995. ISSN: 1055-9965. CODEN: CEBPE4. Pub. Country: United States. Language: English. Summary Language: English.

AB Lignans and isoflavonoids are diphenolic compounds found in plant foods, particularly whole grains and legumes. They have been shown to have anticarcinogenic properties in animal and cell studies, and have been associated with reduced cancer risk in epidemiological studies. In order to perform further epidemiological and metabolic studies on these compounds, it is necessary to be able to monitor concentrations in biological samples. In this study, we examined the effects of consumption of flaxseed, a concentrated source of lignans, on fecal lignan excretion and evaluated the effect of high lignan consumption on fecal excretion of isoflavonoids. Thirteen women were studied for two diet periods of three menstrual cycles each in a cross-over design. During the control period, they consumed their usual diets; during the treatment period they consumed their usual diets supplemented with 10 g/day ground flaxseed. Feces were collected on days 7- 11 of the last menstrual cycle in each diet period. Five-day fecal composites were analyzed for lignans and isoflavonoids by isotope dilution gas chromatography-mass spectrometry. Fecal excretion of the lignans enterodiol, enterolactone, and matairesinol increased significantly with flax consumption, from 80.0 .+-. 80.0 (SD) to 2560 .+-. 3100; 640 .+-. 480 to 10,300 .+-. 7580; and 7.33 .+-. 10.0 to 11.9 .+-. 8.06 nmol/day, respectively. There were no differences in fecal excretion of the isoflavonoids, daidzein, equal, genistein, and O-demethylangolensin.

CT EMTAGS: **malignant neoplastic disease** (0306); therapy (0160); pharmacokinetics (0194); mammal (0738); human (0888); female (0042); human experiment (0104); normal human (0800); controlled study (0197); human tissue, cells or cell components (0111); adult (0018); priority journal (0007); article (0060)

Medical Descriptors:
***food composition**
***cancer inhibition**
cancer risk
diet supplementation
menstrual cycle
feces composition
drug bioavailability
drug metabolism
human
female
human experiment
normal human
clinical trial
randomized controlled trial
crossover procedure
controlled study
human tissue
human cell
adult
priority journal
article

Drug Descriptors:
*lignan: CT, clinical trial
*lignan: PK, pharmacokinetics
*isoflavonoid: AN, drug analysis
*isoflavonoid: CT, clinical trial
*isoflavonoid: PK, pharmacokinetics
*linseed oil: PD, pharmacology

daidzein: AN, drug analysis
daidzein: CT, clinical trial
daidzein: PK, pharmacokinetics
genistein: AN, drug analysis
genistein: CT, clinical trial
genistein: PK, pharmacokinetics
enterolactone: AN, drug analysis
enterolactone: CT, clinical trial
enterolactone: PK, pharmacokinetics
matairesinol: AN, drug analysis
matairesinol: CT, clinical trial
matairesinol: PK, pharmacokinetics
unclassified drug
enterodiol: AN, drug analysis
enterodiol: CT, clinical trial
enterodiol: DV, drug development
enterodiol: PK, pharmacokinetics
equol: AN, drug analysis
equol: CT, clinical trial
equol: DV, drug development
equol: PK, pharmacokinetics
norangolensin: AN, drug analysis
norangolensin: CT, clinical trial
norangolensin: DV, drug development
norangolensin: PK, pharmacokinetics

L109 ANSWER 32 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95311188 EMBASE Protein kinases and phosphatases that act on histidine, lysine, or arginine residues in eukaryotic proteins: A possible regulator of the mitogen-activated protein kinase cascade. Matthews H.R.. Department of Biological Chemistry, University of California, Davis, CA 95616, United States. Pharmacology and Therapeutics 67/3 (323-350) 1995. ISSN: 0163-7258. CODEN: PHTHDT. Pub. Country: United States. Language: English. Summary Language: English.
AB Phosphohistidine goes undetected in conventional studies of protein phosphorylation, although it may account for 6% of total protein phosphorylation in eukaryotes. Procedures for studying protein N-kinases are described. Genes whose products are putative protein histidine kinases occur in a yeast and a plant. In rat liver plasma membranes, activation of the small G-protein, Ras, causes protein histidine phosphorylation. Cellular phosphatases dephosphorylate phosphohistidine. One eukaryotic protein histidine kinase has been purified, and specific proteins phosphorylated on histidine have been observed. There is a protein arginine kinase in mouse and protein lysine kinases in rat. Protein phosphohistidine may regulate the mitogen-activated protein kinase cascade.
CT EMTAGS: chemical procedures (0107); nonhuman (0777); priority journal (0007); review (0001); enzyme (0990)
Medical Descriptors:
*protein phosphorylation
*signal transduction
cell proliferation
eukaryote
nonhuman
priority journal
review
Drug Descriptors:
*protein kinase: EC, endogenous compound
*phosphatase: EC, endogenous compound
*histidine
***lysine**
*enzyme inhibitor
*arginine
*protein kinase inhibitor: PD, pharmacology
*protein kinase inhibitor: DV, drug development
mitogenic agent
genistein: PD, pharmacology

L109 ANSWER 33 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.

95367734 EMBASE Altered time course of urinary daidzein and genistein excretion during chronic soya diet in healthy male subjects. Lu L.-J.W.; Grady J.J.; Marshall M.V.; Ramanujam V.M.S.; Anderson K.E.. Preventive Med./Comm. Health Dept., 2.102 Ewing Hall, University of Texas Medical Branch, Galveston, TX 77555, United States. Nutrition and Cancer 24/3 (311-323) 1995. ISSN: 0163-5581. CODEN: NUCADQ. Pub. Country: United States. Language: English. Summary Language: English.

AB Soybean consumption is associated with reduced rates of prostate and other cancers, possibly due in part to the presence of isoflavones. The metabolism and disposition of these soya-derived phytoestrogens after chronic soya exposure were studied on a metabolic unit in six healthy males (21-35 yrs of age) who consumed an unrestricted hospital diet and a 12-oz portion of soymilk with each meal for one month. The daily isoflavone intake was about 100 mg of daidzein (mostly as daidzin) and about 100 of mg of genistein (mostly as genistin). At two-week intervals, excretion of isoflavones in urine was studied, during which time the subjects consumed a constant basal diet for three to four days, ingested the full daily 36-oz portion of soymilk within 30 minutes each day for one to two days, and collected urine continuously. The urinary recovery of ingested daidzin plus daidzein (46.9 .+-. 15.2% mean .+-. SD) and genistin plus genistein (14.6 .+-. 9.2%) did not change with prolonged soya ingestion. The absorption half-lives (t(1/2)) for daidzein and genistein and the appearance t(1/2) for equol (1 subject) were initially 1.5 .+-. 0.4, 1.9 .+-. 0.6, and 2.2 hours, respectively, and 2.5 .+-. 1.1 (p = 0.06 compared with baseline), 1.4 .+-. 0.9 (p = 0.03 compared with baseline), and 4.2 hours, respectively, during one month of soymilk ingestion. The excretion t(1/2) for daidzein, genistein, and equol were initially 2.9 .+-. 0.5, 3.8 .+-. 0.7, and 5.2 hours, respectively, and 3.9 .+-. 1.2 (p = 0.03), 5.5 .+-. 1.6 (p = 0.02), and 9.7 hours, respectively, during one month of soymilk ingestion. These results indicate that chronic soya exposure did not induce significant changes in the metabolic pathways of isoflavones but altered the time courses of daidzein and genistein excretion. Thus chronic exposure to soya might prolong the tissue exposure to the presumed biologically active free and unconjugated forms of these isoflavones and thereby enhance their oncoprotective effects.

CT EMTAGS: higher plant (0697); plant (0699); therapy (0160); prevention (0165); **malignant neoplastic disease** (0306); mammal (0738); human (0888); male (0041); human experiment (0104); normal human (0800); controlled study (0197); adult (0018); oral drug administration (0181); article (0060); pharmacokinetics (0194)
Medical Descriptors:
***soybean**
*cancer prevention
***cancer inhibition**
urinary excretion
drug urine level
gas chromatography
diet
human
male
human experiment
normal human
controlled study
adult
oral drug administration
article
Drug Descriptors:
*isoflavone derivative: CR, drug concentration
*isoflavone derivative: PK, pharmacokinetics
***genistein: CR, drug concentration**
***genistein: PK, pharmacokinetics**
***daidzein: CR, drug concentration**
***daidzein: PK, pharmacokinetics**
unclassified drug
equol: CR, drug concentration
equol: PK, pharmacokinetics

L109 ANSWER 34 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95318417 EMBASE Inhibition of 5.alpha.-reductase in genital skin fibroblasts and prostate tissue by dietary lignans and isoflavonoids. Evans B.A.J.; Griffiths K.; Morton M.S.. Department of Child Health, University of Wales, College of Medicine, Heath Park, Cardiff CF4 4XN, United Kingdom. Journal of Endocrinology 147/2 (295-302) 1995. ISSN: 0022-0795. CODEN: JOENAK. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Isoflavonoids and lignans, constituents of many plant foods, have been preposed as protective agents in those populations with a low incidence of hormone-dependent cancers. They may act by their inhibition of the metabolism of growth-promoting steroid hormones. This report describes the inhibition of 5.alpha.-reductase and 17.beta.-hydroxysteroid dehydrogenase by six isoflavonoids and two lignans in human genital skin fibroblast monolayers and homogenates, and in benign prostatic hyperplasia tissue homogenates. In genital skin fibroblasts, genistein, biochanin A and equol were the most potent inhibitors of 5.alpha.-reductase activity, each resulting in greater than 80% inhibition at a concentration of 100 .mu.M. The IC50 values for genistein and a seven-compound mixture were approximately 35 .mu.M and 20 .mu.M (2.9 .mu.M of each compound) respectively. Of the lignans, enterolactone was the most potent inhibitor. Inhibition by biochanin A was shown to be reversible. When genital skin fibroblast homogenates were used, biochanin A was found to inhibit 5.alpha.-reductase isozymes 1 and 2 to differing extents (30% and 75% respectively). Genistein was shown to inhibit 5.alpha.-reductase 2 in a non-competitive nature (V(max) and K(m) values without and with inhibitor were 30 and 20 pmol/mg protein per h and 177 and 170 nM respectively). All of the compounds tested inhibited 17.beta.-hydroxysteroid dehydrogenase activity in genital skin fibroblast monolayers. When prostate tissue homogenates were used, the compounds tested were better inhibitors of 5.alpha.-reductase 1 than 2. It is possible that a life-long dietary exposure to these lignans and isoflavonoids may have a significant influence on the development of hormone-dependent tumours.

CT EMTAGS: male genital system (0956); etiology (0135); mammal (0738); human (0888); controlled study (0197); normal human (0800); human tissue, cells or cell components (0111); male (0041); priority journal (0007); article (0060); enzyme (0990)
Medical Descriptors:
*fibroblast
*prostate
***carcinogenesis: ET, etiology**
*hormone dependence
diet
human
controlled study
normal human
human cell
male
priority journal
article
Drug Descriptors:
testosterone 17beta dehydrogenase: EC, endogenous compound
lignan
genistein
biochanin a
enterolactone
unclassified drug
steroid 5alpha reductase: EC, endogenous compound
isoflavonoid
equol

L109 ANSWER 35 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95148619 EMBASE Matrix metalloproteinase-2 and tissue inhibitor of metalloproteinase-2 expression in paediatric tumour cells. Effects of tumour cell proliferation modulators on gelatinolytic activity. Garcia de Veas R.; Schweigerer L.; Medina M.A.. Laboratorio

Bioquimica, Facultad de Ciencias, Universidad Malaga, E-29071 Malaga, Spain. Journal of Cancer Research and Clinical Oncology 121/5 (275-278) 1995. ISSN: 0171-5216. CODEN: JCROD7. Pub. Country: Germany, Federal Republic of. Language: English. Summary Language: English.

AB We have examined the expression of 72-kDa gelatinase/type IV collagenase or matrix metalloproteinase-2 (MMP-2) and its inhibitor, tissue inhibitor of metalloproteinase-2 (TIMP-2), in various cell lines derived from paediatric tumours. In a neuroblastoma model system of tumour progression, the expression level of MMP-2 mRNA was higher in the more malignant cell line. Surprisingly, MMP-2 was not expressed in the highly malignant rhabdomyosarcoma A-204 cell line. TIMP-2 showed higher expression levels in the 007 and U-2OS tumour cell lines than in the more malignant ones, WAC2 and A-204 cells. We have also determined the effect of some tumour cell proliferation modulators on gelatinolytic activity. While basic fibroblast growth factor and retinoic acid produced no apparent change in gelatinolytic activity, genistein induced in partial inhibition of gelatinolytic activity.

CT EMTAGS: malignant neoplastic disease (0306); mammal (0738); human (0888); controlled study (0197); human tissue, cells or cell components (0111); child (0022); priority journal (0007); article (0060); therapy (0160); enzyme (0990)
Medical Descriptors:
*childhood cancer
tumor cell line
gene expression
human
controlled study
human cell
child
priority journal
article
Drug Descriptors:
*tissue inhibitor of metalloproteinase: EC, endogenous compound
***genistein: PD, pharmacology**
***genistein: CM, drug comparison**
*gelatinase: EC, endogenous compound
***retinoic acid: PD, pharmacology**
***retinoic acid: CM, drug comparison**
*basic fibroblast growth factor: PD, pharmacology
*basic fibroblast growth factor: CM, drug comparison
unclassified drug
metalloproteinase 2: EC, endogenous compound

L109 ANSWER 36 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95051598 EMBASE Effect of biochanin A or testosterone on liver tumors induced by a combined treatment of DEN and fission neutron in BCF1 mice. Ogundigie P.O.; Roy G.; Kanin G.; Goto T.; Ito A.. Dept. Cancer Res., Hiroshima Univ., Research Institute, Radiation Biology and Medicine, Kasumi 1-2-3, Minami-ku, Hiroshima 734, Japan. Oncology Reports 2/2 (271-275) 1995. ISSN: 1021-335X. CODEN: OCRPEW. Pub. Country: Greece. Language: English. Summary Language: English.

AB To determine the biological effect of biochanin A, miso or NaCl and sexual influence of testosterone on liver tumor induction, male and female BCF1 mice were i.p. injected once with DEN at a dose of 5 .mu.g/g body weight at 15 days of age. In order to shorten the latency of liver tumor occurrence, the whole body of mice were exposed to 2 Gy of 252Cf fission neutrons at four weeks of age. Three days later, female mice were surgically ovariectomized and given the various doses of testosterone melted into a cholesterol pellet. Male mice were fed on 10 ppm, 20 ppm biochanin A, 10% miso or 2% NaCl supplemented diet for 8 weeks (from 21 to 28 weeks of age) and 4 weeks (from 32 to 36 weeks of age). All mice were sacrificed at 40 weeks of age. Multiplicity of liver tumors was expressed in four different size ranges by <2, 3-5, 6-10 and >10 mm2. Incidence of liver tumors in all experimental groups except in group 1 at 20 weeks were observed at 100%. Average tumor size and

multiplicity were smaller at 20 weeks compared to those of 40-week groups. Male groups fed 20 ppm biochanin A and 2% NaCl had an increase in body weight with significant difference from control by $p < 0.01$. Liver weights were more-or-less the same in all groups except an increase was seen in the group of 20 ppm biochanin A ($p < 0.01$). In female groups, both 0.2 mg and 1 mg of testosterone administration resulted in an increase of tumor multiplicities and a decrease of liver weight compared to that of control group with significant differences. In both male and female groups, majority of liver tumor sizes were in the range of 3-5 mm2. Tumor multiplicities and size in less than 2 mm2 in biochanin A groups, 10% miso and 2% NaCl decreased significantly from control group. These findings suggest that 15-20 weeks is the time in which 1-2 mm2 size of liver tumors start to appear. Among others, biochanin A is a component of miso. The potent anti-tumorigenic effect of dietary miso for mouse liver tumorigenesis may be strenghtened by a combination of factors such as the presence of Biochanin A, protease inhihitors and various fermented enzymes.

CT EMTAGS: etiology (0135); **malignant neoplastic disease** (0306); sex difference (0040); therapy (0160); nonhuman (0777); mouse (0727); mammal (0738); controlled study (0197); animal experiment (0112); animal model (0106); biological model (0502); male (0041); female (0042); oral drug administration (0181); subcutaneous drug administration (0183); priority journal (0007); article (0060); higher plant (0697); plant (0699); radioisotope (0131)

Medical Descriptors:
***liver carcinogenesis**
***cancer inhibition**
diet
neutron radiation
sex difference
liver cancer: DT, drug therapy
nonhuman
mouse
controlled study
animal experiment
animal model
male
female
oral drug administration
subcutaneous drug administration
priority journal
article
ovariectomy

Drug Descriptors:
***biochanin a: DT, drug therapy**
***soybean**
*testosterone: DT, drug therapy
diethylnitrosamine: TO, drug toxicity
cholesterol
californium 252

L109 ANSWER 37 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.

95367730 EMBASE Soybean isoflavone extract suppresses early but not later promotion of hepatocarcinogenesis by phenobarbital in female rat liver. Lee K.-W.; Wang H.-J.; Murphy P.A.; Hendrich S.. Food Science/Human Nutrition Dept., Iowa State University, Ames, IA 50011, United States. Nutrition and Cancer 24/3 (267-278) 1995. ISSN: 0163-5581. CODEN: NUCADQ. Pub. Country: United States. Language: English. Summary Language: English.

AB The antioxidant and anticarcinogenic activities of soybean isoflavone extracts were investigated in female F344/N rats. Diethylnitrosamine (DEN, 15 mg/kg body wt) as a cancer initiator was injected intraperitoneally into 120 female F344/N rats at 10 days of age, and at weaning, phenobarbital (PB, 500 mg/kg diet) was fed to one-half of the rats. Soybean isoflavones were extracted in acetone-0.1 N HCl and analyzed by high-performance liquid chromatography, and two levels of soybean isoflavones (920 and 1,840

.mu.mol/kg diet) were fed during PB treatment for 3 and 11 months. Control rats were fed diets without PB and with or without isoflavones. The effect of soybean isoflavone extract on hepatic glutathione peroxidase was measured, and development of .gamma.-glutamyltransferase (GGT)-positive (GGT+) and placental glutathione transferase (PGST)-positive (PGST+) altered hepatic foci (AHF) was analyzed by computerized stereology. Soybean isoflavone extract providing 920 or 1,840 .mu.mol/kg diet normalized total hepatic glutathione peroxidase activity, which was suppressed about 17% by PB ($p < 0.05$), and both doses of isoflavone extract suppressed PB promotion of hepatocarcinogenesis, decreasing the volume occupied by GGT+ and PGST+ AHF ($p < 0.05$) after three months. After 11 months of PB promotion, isoflavone extract at 920 .mu.mol/kg diet decreased PGST+ AHF compared with the PB-fed group, but neither dose of isoflavone extract suppressed development of GGT+ AHF compared with the group fed PB alone. Furthermore the control group fed isoflavone extract at 1,840 .mu.mol/kg diet showed greater development of GGT+ and PGST+ AHF than the group fed the basal diet alone. Therefore soybean isoflavones may be anticarcinogenic, but their margin of safety is relatively narrow, with a cancer-promoting dose of 1,840 .mu.mol/kg in female F344/N rats initiated with DEN.

CT EMTAGS: etiology (0135); **malignant neoplastic disease** (0306); therapy (0160); prevention (0165); higher plant (0697); plant (0699); nonhuman (0777); female (0042); rat (0733); mammal (0738); animal model (0106); biological model (0502); controlled study (0197); animal tissue, cells or cell components (0105); article (0060); enzyme (0990)
Medical Descriptors:
***liver carcinogenesis**
***liver carcinoma: DT, drug therapy**
***liver carcinoma: PC, prevention**
antineoplastic activity
cancer inhibition
cancer prevention
diet therapy
soybean
nonhuman
female
rat
animal model
controlled study
animal tissue
article
Drug Descriptors:
*isoflavone derivative: DO, drug dose
*isoflavone derivative: DT, drug therapy
*isoflavone derivative: PD, pharmacology
*phenobarbital: DO, drug dose
***daidzein: DO, drug dose**
***daidzein: DT, drug therapy**
***daidzein: PD, pharmacology**
***genistein: DO, drug dose**
***genistein: DT, drug therapy**
***genistein: PD, pharmacology**
glutathione peroxidase: EC, endogenous compound
gamma glutamyltransferase: EC, endogenous compound
tamoxifen: PD, pharmacology

L109 ANSWER 38 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95368644 EMBASE The nonhuman primate model of the relationship between gonadal steroids and coronary heart disease. Clarkson T.B.; Hughes C.L.; Klein K.P.. DVM, Comparative Med. Clinical Res. Ctr., Bowman Gray School of Medicine, Medical Center Blvd, Winston-Salem, NC 27157-1040, United States. Progress in Cardiovascular Diseases 38/3 (189-198) 1995. ISSN: 0033-0620. CODEN: PCVDAN. Pub. Country: United States. Language: English. Summary Language: English.

AB Experimental data derived from studies using cynomolgus macaque females provide strong evidence that estrogen influences both

premenopausal and postmenopausal coronary artery atherosclerosis. Because the monkey studies are not hampered by selection bias, the data are supportive of the tentative conclusions from epidemiological studies indicating that the association between postmenopausal estrogen use and reduced coronary artery atherosclerosis is real. Present forms of HRT are not sufficiently acceptable to women to result in a compliance rate likely to affect the adverse impact of estrogen deprivation on coronary artery atherosclerosis. Nutritional supplementation may provide a more acceptable alternative.

CT EMTAGS: therapy (0160); prevention (0165); mammal (0738); age (0020); etiology (0135); pregnancy (0030); human (0888); nonhuman (0777); female (0042); oral drug administration (0181); review (0001); adverse drug reaction (0198); iatrogenic disease (0300)
Medical Descriptors:
*ischemic heart disease: DT, drug therapy
*ischemic heart disease: PC, prevention
*coronary artery atherosclerosis: DT, drug therapy
*coronary artery atherosclerosis: PC, prevention
macaca
postmenopause
estrogen therapy
atherogenesis
ovariectomy
breast cancer
mastalgia: SI, side effect
depression: SI, side effect
nutrition
pregnancy
diet
stress
human
nonhuman
female
oral drug administration
review
Drug Descriptors:
*estradiol: CB, drug combination
*estradiol: DT, drug therapy
*estradiol: EC, endogenous compound
*conjugated estrogen: DO, drug dose
*conjugated estrogen: DT, drug therapy
*medroxyprogesterone acetate: DO, drug dose
*medroxyprogesterone acetate: DT, drug therapy
***daidzein**
***genistein**
steroid: DT, drug therapy
steroid: EC, endogenous compound
lipoprotein: EC, endogenous compound
high density lipoprotein cholesterol: EC, endogenous compound
ethinylestradiol plus norgestrel: AD, drug administration
ethinylestradiol plus etynodiol diacetate: AD, drug administration
norgestrel
gestagen: AE, adverse drug reaction
cholesterol: EC, endogenous compound
ethinylestradiol plus levonorgestrel: DO, drug dose
progesterone: CB, drug combination
apolipoprotein a1: EC, endogenous compound
apolipoprotein b: EC, endogenous compound
low density lipoprotein: EC, endogenous compound
soybean protein
casein

L109 ANSWER 39 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95260924 EMBASE Rationale for the use of genistein-containing soy matrices in chemoprevention trials for breast and prostate cancer.
Barnes S.; Peterson T.G.; Coward L.. Department of Pharmacology, Birmingham Medical Center, University of Alabama, 1670 University Boulevard, Birmingham, AL 35294-0019, United States. Journal of

Cellular Biochemistry 58/SUPPL. 22 (181-187) 1995. ISSN: 0730-2312. CODEN: JCEBD5. Pub. Country: United States. Language: English. Summary Language: English.

AB Pharmacologists have realized that tyrosine kinase inhibitors (TKI) have potential as anti-cancer agents, both in prevention and therapy protocols. Nonetheless, concern about the risk of toxicity caused by synthetic TKIs restricted their development as chemoprevention agents. However, a naturally occurring TKI (the isoflavone genistein) in soy was discovered in 1987. The concentration of genistein in most soy food materials ranges from 1-2 mg/g. Oriental populations, who have low rates of breast and prostate cancer, consume 20-80 mg of genistein/day, almost entirely derived from soy, whereas the dietary intake of genistein in the US is only 1-3 mg/day. Chronic use of genistein as a chemopreventive agent has an advantage over synthetic TKIs because it is naturally found in soy foods. It could be delivered either in a purified state as a pill (to high-risk, motivated patient groups), or in the form of soy foods or soy-containing foods. Delivery of genistein in soy foods is more economically viable ($1.50 for a daily dose of 50 mg) than purified material ($5/day) and would require no prior approval by the FDA. Accordingly, investigators at several different sites have begun or are planning chemoprevention trials using a soy beverage product based on SUPRO(TM), an isolated soy protein manufactured by Protein Technologies International of St. Louis, MO. These investigators are examining the effect of the soy beverage on surrogate intermediate endpoint biomarkers (SIEBs) in patients at risk for breast and colon cancer, defining potential SIEBs in patients at risk for prostate cancer, and determining whether the soy beverage reduces the incidence of cancer recurrence. These studies will provide the basis for formal Phase I, Phase II and Phase III clinical trials of genistein and soy food products such as SUPRO(TM) for cancer chemoprevention.

CT EMTAGS: therapy (0160); prevention (0165); higher plant (0697); plant (0699); economic aspect (0139); chemical procedures (0107); mammal (0738); human (0888); human tissue, cells or cell components (0111); priority journal (0007); conference paper (0061); enzyme (0990)

Medical Descriptors:
*cancer prevention
***prostate cancer: PC, prevention**
***breast cancer: PC, prevention**
soybean
dietary intake
cost benefit analysis
cancer risk
drug mechanism
protein phosphorylation
cell differentiation
enzyme inhibition
angiogenesis
antioxidant activity
human
human cell
priority journal
conference paper

Drug Descriptors:
*protein tyrosine kinase: EC, endogenous compound
*protein kinase inhibitor: DV, drug development
*protein kinase inhibitor: PD, pharmacology
***genistein: DV, drug development**
***genistein: PD, pharmacology**
*soybean protein: DV, drug development
*soybean protein: PD, pharmacology
estrogen: EC, endogenous compound
tamoxifen: IT, drug interaction
tamoxifen: PD, pharmacology
gyrase inhibitor: PD, pharmacology
isoflavone: AN, drug analysis
isoflavone: DV, drug development

isoflavone: PD, pharmacology
daidzein: AN, drug analysis
daidzein: DV, drug development
daidzein: PD, pharmacology
unclassified drug
protein tyrosine kinase inhibitor: DV, drug development
protein tyrosine kinase inhibitor: PD, pharmacology
supro

L109 ANSWER 40 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95249513 EMBASE A urinary profile study of dietary phytoestrogens. The identification and mode of metabolism of new isoflavonoids. Joannou G.E.; Kelly G.E.; Reeder A.Y.; Waring M.; Nelson C.. Laboratoire de Biochimie Medicale, U.F.R. de Medecine, Universite d'Auvergne, BP 38, 63001 Clermont-Ferrand, France. Journal of Steroid Biochemistry and Molecular Biology 54/3-4 (167-184) 1995. ISSN: 0960-0760. CODEN: JSBBEZ. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB The metabolic fate of the dietary isoflavones daidzein and genistein was investigated in human volunteers challenged with soya. Urinary diphenols, isolated by partition chromatography on Sephadex LH-20, were characterized and identified by profile capillary gas chromatography (GC) and electron ionization mass spectrometry (GC-EIMS) analysis of the trimethylsilyl ether (TMS) derivatives. Novel isoflavonic phytoestrogens found in the urine of volunteers were those of tetrahydrodaidzein, dihydrogenistein, 6'-hydroxy-O-demethylangolensin and 2-dehydro-O-demethylangolensin. Other known diphenols identified were those of equol, dehydrodaidzein, O-demethylangolensin, daidzein, genistein, glycitein, and the lignan enterolactone. Two other urinary isomers with a fragmentation pattern closely resembling that of the persilylated TMS ethers of cis/trans-isomers of tetrahydrodaidzein, were characterized based on the elucidation of fragments associated with the loss of a non-phenolic-OTMS functional group in ring-C. These are fragments presented in the persilylated mass spectra of isoflavan-4-ols and isoflav-3-ene-4-ols, demonstrated here by a combination of simple and tandem mass spectrometry study of the deuterated persilylated TMS ethers of dihydrodaidzein. In a similar study we also present the data on the structural identification and fragment elucidation of the keto/enol tautomers of the TMS ether derivatives of the dihydro derivatives of daidzein and genistein, observed in the urine of volunteers and considered probable products of the derivatization process. Finally, the GC and GC-MS data of two unknown isoflavonoids and that of a lignan-like compound are presented together with those of dihydrodaidzein, dihydrogenistein, tetrahydrodaidzein and 2-dehydro-O-demethylangolensin. The latter four were obtained here as products of small scale chemical synthesis in a preliminary study on the tentative identification of urinary isoflavonoids in human volunteers challenged with soya.

CT EMTAGS: pharmacokinetics (0194); mammal (0738); human (0888); normal human (0800); human tissue, cells or cell components (0111); male (0041); female (0042); adult (0018); article (0060)
Medical Descriptors:
***diet**
*urinalysis
drug metabolism
gas chromatography
mass spectrometry
drug identification
human
normal human
human tissue
male
female
adult
article
Drug Descriptors:
***daidzein: AN, drug analysis**
***daidzein: PK, pharmacokinetics**

***daidzein: CR, drug concentration**
***genistein: AN, drug analysis**
***genistein: PK, pharmacokinetics**
***genistein: CR, drug concentration**
*drug metabolite: AN, drug analysis
*drug metabolite: CR, drug concentration
*isoflavone derivative: AN, drug analysis
*isoflavone derivative: CR, drug concentration

L109 ANSWER 41 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95273780 EMBASE Genetic damage and the inhibition of 7,12-dimethylbenz[a]anthracene-induced genetic damage by the phytoestrogens, genistein and daidzein, in female ICR mice. Giri A.K.; Lu L.-J.W.. Dept. Prevent. Med. Community Hlth., University of Texas Medical Branch, 700 Strand, Galveston, TX 77555-1110, United States. Cancer Letters 95/1-2 (125-133) 1995. ISSN: 0304-3835. CODEN: CALEDQ. Pub. Country: Ireland. Language: English. Summary Language: English.

AB Populations consuming soybeans have reduced rates of breast, colon and prostate cancer possibly due, in part, to the presence in soybeans of two estrogenic isoflavones, genistein and daidzein. This study investigated the genotoxicity of these soya isoflavones and their interactions with 7,12-dimethylbenz[a]anthracene (DMBA)-induced sister chromatid exchanges (SCE) in bone marrow cells and DNA adduct formations in liver and mammary glands of mice. Groups of female ICR mice were pretreated i.p. with daidzein and/or genistein (10-20 mg/kg per day for 6 days or 50 mg/kg per 12 h for 3 days) or with the solvent, dimethylsulfoxide (DMSO). The mice were implanted with bromodeoxyuridine (BrdU) tablets s.c., and treated with DMBA (50 mg/kg) i.p. and colchicine (4 mg/kg) i.p. 24, 23, and 2 h before sacrifice, respectively. In bone marrow cells, DMBA alone induced 11.73 .+-. 1.42 SCE/cell compared to 4.35 .+-. 0.83 SCE/cell in the DMSO treated controls (P = 0.001). DMBA induced 20% fewer SCE (P < 0.05) in mice pretreated with daidzein, genistein or a combination of genistein and daidzein (6 x 20 mg/kg per day for 6 days) when compared to mice that received no pretreatments. Genistein at 50 mg/kg per 12 h for 3 days also inhibited DMBA-induced SCE by 20%. However, treatment for 3 days with 50 mg/kg per 12 h of genistein or daidzein alone, or a combination of daidzein plus genistein (without DMBA treatment) also induced more SCE than treatment with only the solvent (DMSO, P < 0.05). Pretreatment with both the low and the high doses of daidzein plus genistein or the high dose of genistein reduced the replication index of bone marrow cells when compared to pretreatment with DMSO (P < 0.05). Pretreatment with genistein reduced DMBA-induced DNA adduct formation by 34%, but this was only marginally significant (P = 0.08) due to the large inter-individual variability in adduct levels. These results show that genistein and daidzein suppress SCE and possibly DNA adduct formation induced by the known carcinogen, DMBA. This response to a low dose isoflavone exposure may be partly responsible for the protective effect against endocrine cancers of soya consumption.

CT EMTAGS: heredity (0137); blood and hemopoietic system (0927); higher plant (0697); plant (0699); etiology (0135); nonhuman (0777); female (0042); mouse (0727); mammal (0738); animal experiment (0112); animal model (0106); biological model (0502); controlled study (0197); animal tissue, cells or cell components (0105); priority journal (0007); article (0060)
Medical Descriptors:
*genotoxicity
dna damage
genetic damage
bone marrow cell
cell division
dna adduct
soybean
prostate cancer
colon cancer
sister chromatid exchange

liver carcinogenesis
breast carcinogenesis
nonhuman
female
mouse
animal experiment
animal model
controlled study
animal tissue
priority journal
article
Drug Descriptors:
*7,12 dimethylbenz[a]anthracene
***genistein**
***daidzein**
estrogen derivative
broxuridine
colchicine
carcinogen
isoflavone

L109 ANSWER 42 OF 79 MEDLINE DUPLICATE 2
95199366 Antioxidant and antipromotional effects of the soybean isoflavone genistein. Wei H; Bowen R; Cai Q; Barnes S; Wang Y. (Department of Environmental Health Sciences, University of Alabama at Birmingham 35294..)PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE, (1995 Jan) 208 (1) 124-30. Journal code: PXZ. ISSN: 0037-9727. Pub. country: United States. Language: English.

AB Antioxidant and antipromotional effects of the soybean isoflavone genistein have been studied in HL-60 cells and the mouse skin tumorigenesis model. Effects of structure-related flavone/isoflavones on hydrogen peroxide (H2O2) production by 12-O-tetradecanoylphorbol-13-acetate (TPA)-activated HL-60 cells and superoxide anion (O2-) generation by xanthine/xanthine oxidase were compared. Of tested isoflavones, genistein is the most potent inhibitor among TPA-induced H2O2 formation by (dimethyl sulfoxide) DMSO-differentiated HL-60 cells, daidzein is second, and apigenin and biochanin A show little effect. In contrast, genistein, apigenin, and prunectin are equally potent in inhibiting O2- generation by xanthine/xanthine oxidase, with daidzein showing a moderate inhibitory effect and biochanin A exhibiting no effect. These results suggest that the antioxidant properties of isoflavones are structurally related and the hydroxy group at Position 4' is crucial in both systems. Dietary administration of 250 ppm genistein for 30 days significantly enhances the activities of antioxidant enzymes in the skin and small intestine of mice. Further studies show that genistein significantly inhibits TPA-induced proto-oncogene expression (c-fos) in mouse skin in a dose-dependent manner. In a two-stage skin carcinogenesis study, low levels of genistein (1 and 5 mumol) significantly prolong tumor latency and decrease tumor multiplicity by approximately 50%. We conclude that genistein's antioxidant properties and antiproliferative effects may be responsible for its anticarcinogenic effect. Its high content in soybeans and relatively high bioavailability favor genistein as a promising candidate for the prevention of human cancers.

CT Check Tags: Animal; Female; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Anticarcinogenic Agents: PD, pharmacology
*Antioxidants: PD, pharmacology
Cell Differentiation: DE, drug effects
Flavones: PD, pharmacology
Gene Expression: DE, drug effects
Hydrogen Peroxide: ME, metabolism
Intestine, Small: EN, enzymology
*Isoflavones: PD, pharmacology
Mice
*Proto-Oncogenes: GE, genetics
RNA, Messenger: BI, biosynthesis
Skin: EN, enzymology

Skin Neoplasms: CI, chemically induced
***Skin Neoplasms: PC, prevention & control**
Soybeans: CH, chemistry
Superoxides: ME, metabolism
Tetradecanoylphorbol Acetate: PD, pharmacology
Tumor Cells, Cultured
Xanthine Oxidase: AI, antagonists & inhibitors
9,10-Dimethyl-1,2-benzanthracene: PD, pharmacology

L109 ANSWER 43 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95371433 EMBASE Phytoestrogens are partial estrogen agonists in the adult male mouse. Makela S.; Santti R.; Salo L.; McLachlan J.A.. University of Turku, Institute of Biomedicine, Department of Anatomy, Kiinamyllynkatu 10, FIN-20520 Turku, Finland. Environmental Health Perspectives 103/SUPPL. 7 (123-127) 1995. ISSN: 0091-6765. CODEN: EVHPAZ. Pub. Country: United States. Language: English. Summary Language: English.

AB The intake, as well as serum and urinary concentrations, of phytoestrogens is high in countries where incidence of prostate cancer is low, suggesting a chemopreventive role for phytoestrogens. Their significance could be explained by the ability to antagonize the action of more potent endogenous estrogens in initiation or promotion of tumor formation. We have studied estrogenicity and antiestrogenicity of dietary soy and two phyloestrogens, coumestrol and daidzein, in our neoDES mouse model for the study of prostatic neoplasia. Soy was chosen because it is rich in phytoestrogens, is widely used in Oriental diets, and has antiestrogenic and anticarcinogenic properties in the neoDES mouse when given from fertilization onward. In short-term tests with adult animals, no evidence for estrogenicity or antiestrogenicity (capability to antagonize the action of 17.beta.-estradiol) of soy was found when development of epithelial metaplasia and expression of c-fos protooncogene in prostate were used as end points of estrogen action. Estrogenic activity of coumestrol and daidzein on c-fos expression was subtle. Coumestrol, either given alone or in combination with 17.beta.-estradiol, had no effect on development of epithelial metaplasia. These marginal or missing effects in adult males could be interpreted by assuming that the neonatal period is more critical for estrogenic or antiestrogenic action of soy and phytoestrogens. Once initiated, estrogen-related lesions would develop spontaneously. Alternatively, the chemopreventive action of soy is not due to antiestrogenicity of soy-derived phytoestrogens.

CT EMTAGS: prevention (0165); therapy (0160); higher plant (0697); plant (0699); heredity (0137); nonhuman (0777); male (0041); mouse (0727); mammal (0738); animal experiment (0112); controlled study (0197); animal tissue, cells or cell components (0105); oral drug administration (0181); priority journal (0007); conference paper (0061)
Medical Descriptors:
*estrogen activity
***prostate cancer: PC, prevention**
*cancer prevention
soybean
diet
oncogene c fos
gene expression regulation
nonhuman
male
mouse
animal experiment
controlled study
animal tissue
oral drug administration
priority journal
conference paper
Drug Descriptors:
*phytohormone
*estrogen
*coumestrol: DV, drug development

***daidzein: DV, drug development**
hormone receptor stimulating agent
estradiol

L109 ANSWER 44 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95371431 EMBASE Phytoestrogens: Epidemiology and a possible role in cancer protection. Adlercreutz H.. Department of Clinical Chemistry, University of Helsinki, Meilahti Hospital, FIN-00290 Helsinki, Finland. Environmental Health Perspectives 103/SUPPL. 7 (103-112) 1995. ISSN: 0091-6765. CODEN: EVHPAZ. Pub. Country: United States. Language: English. Summary Language: English.

AB Because many diseases of the Western Hemisphere are hormone-dependent cancers, we have postulated that the Western diet, compared to a vegetarian or semivegetarian diet, may alter hormone production, metabolism or action at the cellular level by some biochemical mechanisms. Recently, our interest has been mainly focused on the cancer-protective role of some hormonelike diphenolic phytoestrogens of dietary origin, the lignans and the isoflavonoids. The precursors of the biologically active compounds originate in soybean products (mainly isoflavonoids), whole grain cereal food, seeds, and probably berries and nuts (mainly lignans). The plant lignan and isoflavonoid glycosides are converted by intestinal bacteria to hormonelike compounds with weak estrogenic but also antioxidative activity; they have now been shown to influence not only sex hormone metabolism and biological activity but also intracellular enzymes, protein synthesis, growth factor action, malignant cell proliferation, differentiation, and angiogenesis in a way that makes them strong candidates for a role as natural cancer-protective compounds. Epidemiologic investigations strongly support this hypothesis because the highest levels of these compounds in the diet are found in countries or regions with low cancer incidence. This report is a review on recent results suggesting that the diphenolic, isoflavonoids and lignans are natural cancer-protective compounds.

CT EMTAGS: therapy (0160); prevention (0165); higher plant (0697); plant (0699); malignant neoplastic disease (0306); epidemiology (0400); mammal (0738); human (0888); nonhuman (0777); male (0041); female (0042); priority journal (0007); conference paper (0061); enzyme (0990)
Medical Descriptors:
***diet**
*cancer prevention
*hormone metabolism
soybean
protein synthesis
cancer growth
angiogenesis
cell differentiation
antineoplastic activity
cancer incidence
hormone blood level
breast cancer: PC, prevention
prostate cancer: PC, prevention
colon cancer: PC, prevention
vegetarian diet
cereal
human
nonhuman
male
female
priority journal
conference paper
Drug Descriptors:
*phytohormone: EC, endogenous compound
*isoflavonoid: EC, endogenous compound
*lignan: EC, endogenous compound
*estrogen
antioxidant
protein: EC, endogenous compound

cell enzyme: EC, endogenous compound
growth factor: EC, endogenous compound
antineoplastic agent: EC, endogenous compound
sex hormone binding globulin: EC, endogenous compound
genistein: EC, endogenous compound

L109 ANSWER 45 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95073790 EMBASE Isotope dilution gas chromatographic-mass spectrometric method for the determination of unconjugated lignans and isoflavonoids in human feces, with preliminary results in omnivorous and vegetarian women. Adlercreutz H.; Fotsis T.; Kurzer M.S.; Wahala K.; Makela T.; Hase T.. Department Clinical Chemistry, University of Helsinki, Meilahti Hospital, FIN-00290 Helsinki, Finland. Analytical Biochemistry 225/1 (101-108) 1995. ISSN: 0003-2697. CODEN: ANBCA2. Pub. Country: United States. Language: English. Summary Language: English.

AB We describe an isotope dilution gas chromatographic-mass spectrometric (GC/MS) method for the identification and quantitative determination of the lignans enterolactone, enterodiol, and matairesinol and the isoflavonoids daidzein, equol, O-desmethylangolensin, and genistein in feces. Following the addition of deuterated internal standards for all compounds, the feces samples are extracted and purified in several ion exchange chromatographic steps. Following formation of trimethylsilyl ethers, the samples are analyzed by combined capillary column GC/MS in the selective ion monitoring mode and corrected for all losses during the procedure using the deuterated internal standards. Results on the reliability of the method and values for nine Finnish omnivorous and nine vegetarian women are presented.

CT EMTAGS: europe (0402); western europe (4021); methodology (0130); mammal (0738); human (0888); controlled study (0197); human experiment (0104); normal human (0800); human tissue, cells or cell components (0111); female (0042); aged (0019); adult (0018); priority journal (0007); article (0060)
Medical Descriptors:
*feces analysis
vegetarian diet
diet
isotope dilution assay
finland
gas chromatography
mass spectrometry
methodology
quantitative assay
human
controlled study
human experiment
normal human
human tissue
clinical trial
female
aged
adult
priority journal
article
Drug Descriptors:
*lignan: EC, endogenous compound
*isoflavonoid: EC, endogenous compound
enterolactone: EC, endogenous compound
matairesinol: EC, endogenous compound
daidzein: EC, endogenous compound
genistein: EC, endogenous compound
unclassified drug
enterodiol: EC, endogenous compound
norangolensin: EC, endogenous compound

L109 ANSWER 46 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95042605 EMBASE Lignan and isoflavonoid conjugates in human urine. Adlercreutz H.; Van der Wildt J.; Kinzel J.; Attalla H.; Wahala K.;

Makela T.; Hase T.; Fotsis T.. Department of Clinical Chemistry, University of Helsinki, Central Hospital, (Meilahti Hosp.), 00290 Helsinki, Finland. Journal of Steroid Biochemistry and Molecular Biology 52/1 (97-103) 1995. ISSN: 0960-0760. CODEN: JSBBEZ. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Lignans and isoflavonoids are two groups of diphenolic phytoestrogens of plant origin which have gained increasing interest because of their possible cancer protective properties. High excretion of these compounds occur in populations at low risk of breast, prostate and colon cancer consuming either high amounts of whole-grain (lignans and some isoflavonoids) or soy products (isoflavonoids and some lignans). We determined the pattern of conjugation of the phytoestrogens in four urine samples from vegetarian or semivegetarian women and in two samples from men. Seven compounds were investigated: enterodiol, enterolactone, matairesinol, daidzein, equol, genistein and O-desmethylangolensin. The fractions quantified are the free fraction, mono- and disulfate, as well as the mono-, di- and sulfoglucuronide fractions. For the fractionation and purification we used ion-exchange chromatography and the determination of the concentrations of each compound in all fractions was done by isotope dilution gas chromatography-mass spectrometry (GLC-MS) using deuterated internal standards of all diphenols. More than 60% of all compounds determined, occurred in the monoglucuronide fraction. Daidzein, enterodiol and equol are excreted to a relatively high extent as sulfoglucuronides and genistein as diglucuronide. We conclude that the general pattern of lignan and isoiflavonoid conjugates in urine is similar to that of endogenous estrogens.

CT EMTAGS: **malignant neoplastic disease** (0306); chemical procedures (0107); mammal (0738); human (0888); controlled study (0197); human experiment (0104); normal human (0800); male (0041); female (0042); article (0060)
Medical Descriptors:
***cancer**
*urinalysis
*metabolism
sulfation
glucuronidation
gas chromatography
mass spectrometry
risk factor
diet
vegetarian
human
controlled study
human experiment
normal human
male
female
article
Drug Descriptors:
*lignan: EC, endogenous compound
*isoflavonoid: EC, endogenous compound
*enterolactone: EC, endogenous compound
***genistein: EC, endogenous compound**
*matairesinol: EC, endogenous compound
***daidzein: EC, endogenous compound**
unclassified drug
enterodiol: EC, endogenous compound
norangolensin: EC, endogenous compound
equol: EC, endogenous compound

L109 ANSWER 47 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95009577 EMBASE Rapid HPLC analysis of dietary phytoestrogens from legumes and from human urine. Franke A.A.; Custer L.J.; Cerna C.M.; Narala K.. Molecular Carcinogenesis Program, Cancer Research Center of Hawaii, 1236 Lauhala Street, Honolulu, HI 96813, United States. Proceedings of the Society for Experimental Biology and Medicine

208/1 (18-26) 1995. ISSN: 0037-9727. CODEN: PSEBAA. Pub. Country: United States. Language: English. Summary Language: English.

AB Due to growing evidence suggesting that phytoestrogens might protect against various cancers, particularly against breast and prostate cancer, it is important to measure the exposure of populations to these compounds by determining levels in food and in human tissue or body fluids to assess the possible cancer protective properties of these agents. Therefore, we developed a simple and fast procedure to extract and simultaneously hydrolyze phytoestrogens and their conjugates from food items, and present a fast and selective high-performance liquid chromatography (HPLC) method for precise determinations of the most common dietary phytoestrogens genistein, biochanin-A, daidzein, formononetin, and coumestrol using flavone as internal standard. For the first time HPLC was applied to measure these phytoestrogens and their most abundant metabolites equol and O-desmethyl-angotensin from human urine. The proposed methodology has been evaluated for losses due to thermal degradation during extraction and hydrolysis and due to sample handling during the entire work-up including solid phase extraction, and values are given for inter- and intra-assay variability. We present isoflavonoid levels of most common peas and beans used in 'western' and 'eastern' diets and compare isoflavonoid and coumestrol levels of raw, canned, and cooked foods which can be used in future epidemiological studies. We also determined human urinary levels with our methodology comparing values before and after soybean intake.

CT EMTAGS: higher plant (0697); plant (0699); methodology (0130); mammal (0738); human (0888); nonhuman (0777); controlled study (0197); conference paper (0061)
Medical Descriptors:
*high performance liquid chromatography
chemical analysis
extraction
hydrolysis
urine level
legume
metabolite
food analysis
technique
human
nonhuman
controlled study
conference paper
Drug Descriptors:
*phytohormone: CR, drug concentration
*phytohormone: DV, drug development
*estrogen derivative: CR, drug concentration
*estrogen derivative: DV, drug development
genistein: CR, drug concentration
genistein: DV, drug development
biochanin a: CR, drug concentration
biochanin a: DV, drug development
daidzein: CR, drug concentration
daidzein: DV, drug development
formononetin: CR, drug concentration
formononetin: DV, drug development
coumestrol: CR, drug concentration
coumestrol: DV, drug development
flavone: CR, drug concentration
flavone: DV, drug development

L109 ANSWER 48 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.

94312694 EMBASE Defining food components as new nutrients. Hendrich S.; Lee K.-W.; Xu X.; Wang H.-J.; Murphy P.A.. Food Science and Human Nutrition, Iowa State University, Ames, IA 50011, United States. J. NUTR. 124/9 SUPPL. (1789S-1792S) 1994. ISSN: 0022-3166. CODEN: JONUAI. Pub. Country: United States. Language: English. Summary Language: English.

AB When obtained from a usual diet, a food component that sustains or

enhances physiological functions and/or prevents diseases is a nutrient. Isoflavones, tocotrienols, and carotenoids are candidate nutrients which may be of health benefit to humans by inhibiting cancer development and reducing risk of atherosclerosis. The amounts of some of these candidate nutrients in foods are known. A carotenoid data base has been developed. Isoflavone content of soy foods ranges from 0.1 mg/g (soymilk) to 2.5 mg/g (soy protein isolate). Human bioavailability studies have also been performed with these candidate nutrients. For example, in young adult females fed a single meal containing soy milk, isoflavones were cleared from urine within 24 h after feeding, with about 15-20% of the total dose accounted for in urine and feces. The two major soy isoflavones, genistein and daidzein, differ in bioavailability, with daidzein being more readily excreted in urine. Isoflavones, tocotrienols, and carotenoids meet several criteria for classification as nutrients. But after appropriate animal testing, food analyses, and availability studies have been performed, human health- protective efficacy must be proven in long-term feeding trials, in order for potential health-enhancing food components to be classified as nutrients.

CT EMTAGS: **malignant neoplastic disease** (0306); higher plant (0697); plant (0699); mammal (0738); human (0888); nonhuman (0777); conference paper (0061)
Medical Descriptors:
*atherosclerosis
***malignant neoplastic disease**
food composition
nutrient
food analysis
soybean
nutritional health
bioavailability
human
nonhuman
conference paper
Drug Descriptors:
*isoflavone derivative
***alpha tocotrienol**
***carotenoid**
genistein
daidzein

L109 ANSWER 49 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95011672 EMBASE Daidzin, an antioxidant isoflavonoid, decreases blood alcohol levels and shortens sleep time induced by ethanol intoxication. Xie C.-I.; Lin R.C.; Antony V.; Lumeng L.; Li T.-K.; Mai K.; Liu C.; Wang Q.- D.; Zhao Z.-H.; Wang G.-F.. Department of Medicine, Emerson Hall 421, Indiana University Sch. of Medicine, 545 Barnhill Drive, Indianapolis, IN 46202, United States. Alcoholism: Clinical and Experimental Research 18/6 (1443-1447) 1994. ISSN: 0145-6008. CODEN: ACRSDM. Pub. Country: United States. Language: English. Summary Language: English.

AB The extract from an edible vine, Pueraria lebata, has been reported to be efficacious in lessening alcohol intoxication. In this study, we have tested the efficacy of one of the major components, daidzin, from this plant extract. When ethanol (40% solution, 3 g/kg body weight) was given to fasted rats intragastrically, blood alcohol concentration (BAC) peaked at 30 min offer alcohol ingestion and reached 1.77 .+-. 0.14 mg/ml (mean values .+-. SD, n = 6). If daidzin (30 mg/kg) was mixed with the ethanol solution and given to animals intragastrically, BAC was found to peak at 90 min after alcohol ingestion and reached only 1.20 .+-. 0.30 mg/ml (n = 6) ($p < 0.05$ vs. controls). The ability of daidzin to delay and decrease peak BAC level after ethanol ingestion was also observed in fed animals. In both fasted and fed rats given alcohol without daidzin, BAC quickly declined after reaching its peak at 30 min. By contrast, BAC levels receded more slowly if daidzin was also fed to the animals. Daidzin showed a chronic effect. Rats fed daidzin for 7 days before ethanol challenge, but not on the day of challenge, also

produced lower and later peak BAC levels. Interestingly, daidzin, whether fed to rats only once or chronically for 7 days, did not significantly alter activities of either alcohol dehydrogenase or mitochondrial aldehyde dehydrogenase in the liver. Further experiments demonstrated that daidzin shortened sleep time for rats receiving ethanol intragastrically (7 g/ kg) but not intraperitoneally (2 g/kg). To test whether daidzin delayed stomach-emptying, [14C]polyethylene glycol was mixed with ethanol and fed to rats. It was found that, 30 min after intragastric feeding, more ethanol and [14C]polyethylene glycol remained in the stomach if rats were also given daidzin. Because daidzin is an isoflavonoid glucoside that possesses strong antioxidant activity, two other antioxidants (i.e., vitamin E and thioctic acid) were tested. Similar to daidzin, these two antioxidants also delayed and suppressed peak BAC, as well as shortened sleep time induced by alcohol ingestion. We conclude that: (1) daidzin is effective in countering alcohol intoxication; (2) suppression of BAC by daidzin is due mainly to delay of stomach-emptying, but not to accelerated clearance of ethanol in circulation by liver enzymes; and (3) the effect of daidzin may in part be due to its antioxidant activity.

CT EMTAGS: intoxication (0302); diagnosis (0140); nonhuman (0777); male (0041); rat (0733); mammal (0738); animal model (0106); biological model (0502); controlled study (0197); animal tissue, cells or cell components (0105); intragastric drug administration (0286); intraperitoneal drug administration (0178); priority journal (0007); article (0060)

Medical Descriptors:
*alcohol intoxication: DI, diagnosis
drug effect
antioxidant activity
alcohol blood level
sleep time
drug efficacy
stomach emptying
nonhuman
male
rat
animal model
controlled study
animal tissue
intragastric drug administration
intraperitoneal drug administration
priority journal
article

Drug Descriptors:
***daidzein: AD, drug administration**
***daidzein: PD, pharmacology**
antioxidant: AD, drug administration
antioxidant: PD, pharmacology
isoflavonoid: AD, drug administration
isoflavonoid: PD, pharmacology
alpha tocopherol: PD, pharmacology
thioctic acid: PD, pharmacology
alcohol
plant extract: AD, drug administration
plant extract: PD, pharmacology

L109 ANSWER 50 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.

94364865 EMBASE Potentiation by cholesterol and vitamin D3 oxygenated derivatives of arachidonic acid release and prostaglandin E2 synthesis induced by the epidermal growth factor in NRK 49F cells: The role of protein kinase C. Astruc M.E.; Lahoua Z.. INSERM U. 58, 60 Rue de Navacelles, 34090 Montpellier, France. Cellular Signalling 6/7 (763-775) 1994. ISSN: 0898-6568. CODEN: CESIEY. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB We have previously demonstrated that oxysterols and calcitriol potentiate arachidonic acid (AA) release and prostaglandin (PG) synthesis when NRK cells (fibroblastic clone 49F) are activated by foetal calf serum. As serum is essential for a full oxysterol

effect, we hypothesizes that these compounds could act on one or more of the events triggered by serum growth factor binding to their specific receptors and leading to PLA2 activation; we showed that the oxysterol effect on AA release is synergistic with, but not fully dependent on, protein kinase C (PKC) activity and Ca2+ ion fluxes, suggesting that oxysterols could effect early events in the cell signalling pathway. In the present paper, we investigated the effect of some oxysterols and calcitriol on epidermal growth factor (EGF)-induced AA release and PGE2 synthesis in NRK cells. The clear potentiation of EGF effect by most of the oxygenated sterols - chiefly when polyoxidized - cannot be explained by a modification EGF high affinity binding site number which was only moderately increased after a 4 H incubation of cells with these compounds, and moreover was not related to the ability of a given oxysterol of increase PLA2 activity; whatever the compound, the dissociation constant (K(D)) of either a high or low affinity binding site was unchanges (respectively, 3.5 x 10-11 M and 4.4 x 10-10 M). Genistein, a known inhibitor of EGF receptor tyrosine kinase, changed neither the EGF effect on AA release nor its potentiation by oxysterol, whereas it inhibited PGE2 synthesis in both situations, PKC activation by phorbol ester TPA increased the effect of EGF alone as well as the oxysterol potentiation effect, whereas PKC down-regulation strongly decreased both of these effects, showing that both are dependent on PKC activity. Nevertheless staurosporine, a PKC inhibitor, did not reproduce the effects of PKC down-regulation on EGF activation: stimulatory when AA release was induced by EGF alone, inhibitory when AA release is induced by TPA alone, this compound did not modify the oxysterol potentiating effect. In conclusion, the potentiating effect of oxysterols on AA release seems to be exerted downstream to the growth factor receptor (as demonstrated here with EGF) and probably at the PKC level, but not exclusively.

CT EMTAGS: urinary tract (0950); kidney (0951); nonhuman (0777); rat (0733); mammal (0738); controlled study (0197); animal tissue, cells or cell components (0105); priority journal (0007); article (0060); enzyme (0990); therapy (0160)

Medical Descriptors:
*prostaglandin synthesis
signal transduction
kidney cell
nonhuman
rat
controlled study
animal cell
priority journal
article

Drug Descriptors:
*epidermal growth factor: PD, pharmacology
*protein kinase c: EC, endogenous compound
***colecalciferol derivative: PD, pharmacology**
***colecalciferol derivative: CM, drug comparison**
*arachidonic acid: EC, endogenous compound
*prostaglandin e2: EC, endogenous compound
phospholipase a2: EC, endogenous compound
cholesterol derivative: PD, pharmacology
cholesterol derivative: CM, drug comparison
calcitriol: PD, pharmacology
calcitriol: CM, drug comparison
7alpha hydroxycholesterol: PD, pharmacology
7alpha hydroxycholesterol: CM, drug comparison
7beta hydroxycholesterol: PD, pharmacology
7beta hydroxycholesterol: CM, drug comparison
22 hydroxycholesterol: PD, pharmacology
22 hydroxycholesterol: CM, drug comparison
25 hydroxycholesterol: PD, pharmacology
25 hydroxycholesterol: CM, drug comparison
genistein: IT, drug interaction
genistein: CB, drug combination
genistein: PD, pharmacology

genistein: CM, drug comparison
staurosporine: CB, drug combination
staurosporine: IT, drug interaction
staurosporine: PD, pharmacology
staurosporine: CM, drug comparison
*cholesterol: PD, pharmacology
*cholesterol: CM, drug comparison

L109 ANSWER 51 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
94222217 EMBASE Bioactive substances in food: Identification and potential uses. Kitts D.D.. Department of Food Science, University of British Columbia, Vancouver, BC V6T 1Z4, Canada. CAN. J. PHYSIOL. PHARMACOL. 72/4 (423-434) 1994. ISSN: 0008-4212. CODEN: CJPPA3. Pub. Country: Canada. Language: English. Summary Language: English; French.

AB Bioactive substances in foods can represent 'extranutritional' constituents naturally present in small quantities in the food matrix, produced upon either in vivo or industrial enzymatic digestion, the latter being a result of food-processing activities. Bioactive constituents of food evoke physiological, behavioral, and immunological effects. Evidence from both epidemiological and animal studies has suggested chemopreventative roles for phytochemicals in certain forms of cancers and in the control of hyperlipidemia. Secondary products of plant metabolism can modulate xenobiotic metabolizing and cholesterol synthetic enzymes. Unique physicochemical properties of food-derived peptides with characteristic amino acid composition and sequences have been reported to influence intestinal transit, modify nutrient absorption and excretion, and exhibit immunostimulating and antihypertensive activity. Biologically active peptides derived from casein, fish muscle, and plant protein hydrolysates have been isolated, purified, and identified in peptide sequence studies. Therapeutic proteins (e.g., specific antibodies) derived from animal products such as milk may offer the potential for developing specialized food products with prophylactic as well as nutritive quality. This paper discusses the physicochemical mechanism of action of specific bioactive substances naturally present in or derived from foods. The biotechnologies employed to develop these products and the issues concerning acceptance by consumer and regulatory bodies are also addressed.

CT EMTAGS: **malignant neoplastic disease** (0306); mammal (0738); human (0888); nonhuman (0777); priority journal (0007); conference paper (0061)
Medical Descriptors:
***nutrition**
***food**
*biotechnology
chronic disease
health
behavior
immunity
cancer
hyperlipidemia
intestine absorption
physical chemistry
human
nonhuman
priority journal
conference paper
Drug Descriptors:
***food additive: PD, pharmacology**
peptide: PD, pharmacology
protein: PD, pharmacology
3 indolemethanol: PD, pharmacology
phenol derivative: PD, pharmacology
caffeic acid: PD, pharmacology
chlorogenic acid: PD, pharmacology
ellagic acid: PD, pharmacology
curcumin: PD, pharmacology

flavone derivative: PD, pharmacology
luteolin: PD, pharmacology
quercetin: PD, pharmacology
myricetin: PD, pharmacology
apigenin: PD, pharmacology
genistein: PD, pharmacology
daidzein: PD, pharmacology
limonene: PD, pharmacology
allyl sulfide: PD, pharmacology
unindexed drug
unclassified drug
indole derivative: PD, pharmacology
indole 3 acetonitrile: PD, pharmacology
3,3' diindolylmethane: PD, pharmacology
isothiocyanic acid: PD, pharmacology
formononetin: PD, pharmacology
carvone: PD, pharmacology

L109 ANSWER 52 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
94277549 EMBASE Biological effects of a diet of soy protein rich in isoflavones on the menstrual cycle of premenopausal women. Cassidy A.; Bingham S.; Setchell K.D.R.. Div. of Clinical Mass Spectrometry, Department of Pediatrics, Children's Hospital Medical Center, 3333 Burnet Avenue, Cincinnati, OH 45229, United States. AM. J. CLIN. NUTR. 60/3 (333-340) 1994. ISSN: 0002-9165. CODEN: AJCNAC. Pub. Country: United States. Language: English. Summary Language: English.

AB The influence of a diet containing soy protein on the hormonal status and regulation of the menstrual cycle was examined in six premenopausal women with regular ovulatory cycles. Soy protein (60 g containing 45 mg isoflavones) given daily for 1 mo significantly ($P < 0.01$) increased follicular phase length and/or delayed menstruation. Midcycle surges of luteinizing hormone and follicle-stimulating hormone were significantly suppressed during dietary intervention with soy protein. Plasma estradiol concentrations increased in the follicular phase and cholesterol concentrations decreased 9.6%. Similar responses occur with tamoxifen, an antiestrogen undergoing clinical trial as a prophylactic agent in women at high risk for breast cancer. These effects are presumed to be due to nonsteroidal estrogens of the isoflavone class, which behave as partial estrogen agonists/antagonists. The responses to soy protein are potentially beneficial with respect to risk factors for breast cancer and may in part explain the low incidence of breast cancer and its correlation with a high soy intake in Japanese and Chinese women.

CT EMTAGS: therapy (0160); age (0020); epidemiology (0400); etiology (0135); prevention (0165); Asia (0407); mammal (0738); human (0888); female (0042); human experiment (0104); normal human (0800); controlled study (0197); adult (0018); article (0060)
Medical Descriptors:
***protein diet**
***menstrual cycle**
*premenopause
***breast cancer: DT, drug therapy**
***breast cancer: EP, epidemiology**
***breast cancer: ET, etiology**
***breast cancer: PC, prevention**
follicular phase
luteinizing hormone release
risk factor
estradiol blood level
caloric intake
cholesterol blood level
body weight
japan
chinese people's republic
human
female
human experiment

normal human
clinical trial
controlled study
adult
article
Drug Descriptors:
*soybean protein
*isoflavone
*tamoxifen: CT, clinical trial
*tamoxifen: DT, drug therapy
*estrogen
estradiol: EC, endogenous compound
antiestrogen
follitropin: EC, endogenous compound
luteinizing hormone: EC, endogenous compound
cholesterol: EC, endogenous compound
sex hormone binding globulin: EC, endogenous compound
progesterone: EC, endogenous compound
testosterone: EC, endogenous compound
daidzein
genistein

L109 ANSWER 53 OF 79 MEDLINE DUPLICATE 3
95016346 Determination of lignans and isoflavonoids in human female plasma following dietary supplementation. Morton M S; Wilcox G; Wahlqvist M L; Griffiths K. (Tenovus Cancer Research Centre, University of Wales College of Medicine, Heath Park, Cardiff, UK..)JOURNAL OF ENDOCRINOLOGY, (1994 Aug) 142 (2) 251-9. Journal code: I1J. ISSN: 0022-0795. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Plasma levels of the lignans enterodiol and enterolactone, and also the isoflavonic phyto-oestrogens daidzein, equol and genistein, are reported for postmenopausal Australian women consuming a traditional diet supplemented with linseed, soya flour or clover sprouts. Analysis was performed by gas chromatography-mass spectrometry, after enzymatic hydrolysis and ion-exchange chromatography. Following linseed supplementation, combined levels of enterolactone and enterodiol reached 500 ng/ml, whereas after soya flour or clover sprouts the respective concentrations of equol, daidzein and genistein reached 43, 312 and 148 ng/ml. Not all subjects were able to produce equol from daidzein. The possible relationship and role of these weak dietary oestrogens as restraining factors in the development of hormone-dependent cancers in Asian populations is discussed.

CT Check Tags: Comparative Study; Female; Human; Support, Non-U.S. Gov't
Australia
Chromans: BL, blood
***Diet**
Estrogens: BL, blood
***Food, Fortified**
*Isoflavones: BL, blood
*Lignans: BL, blood
Linseed Oil: AD, administration & dosage
Mass Fragmentography
Middle Age
Monoamine Oxidase Inhibitors: BL, blood
Neoplasms: PC, prevention & control
Plants, Edible
Postmenopause: BL, blood
Soybeans
4-Butyrolactone: AA, analogs & derivatives
4-Butyrolactone: BL, blood

L109 ANSWER 54 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
94284315 EMBASE Characterization of an all trans retinoic acid-resistant HL-60 subline. Li L.; Han R.. Institute of Materia Medica, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing 100850, China. CHIN. J. PHARMACOL. TOXICOL. 8/3

(191-195) 1994. ISSN: 1000-3002. CODEN: ZYYZEW. Pub. Country: China. Language: Chinese. Summary Language: English; Chinese.

AB HL-60/RA, an all trans retinoic acid (RA) resistant subline of human promyelocytic leukemia cell line HL-60 was cloned. The resistance to RA is in a range of 2000 times in HL-60/RA and its resistance could keep for a long period (at least for 18 months) without RA. HL-60/RA was also cross-resistant to other inducers for granulocytic differentiation, such as 1,6-hexamethylene bisacetamide and dimethyl sulfoxide. However, HL-60/RA is not cross-resistant to 12-O-tetradecanoylphorbol-13-acetate, a typical monocyte-macrophage inducer. These results suggest that HL-60/RA is a stable, highly RA-resistant HL-60 subline. This subline could be used as a model for the study of differentiation-resistance of tumor cells and the mechanisms of cell differentiation as well as differentiation-inducers.

CT EMTAGS: reticuloendothelial system (0924); mammal (0738); human (0888); controlled study (0197); human tissue, cells or cell components (0111); article (0060)
Medical Descriptors:
***leukemia cell line**
cell strain hl 60
drug resistance
cross resistance
cell structure
cell differentiation
phagocyte
concentration response
human
controlled study
human cell
article
Drug Descriptors:
***retinoic acid**
dimethyl sulfoxide: PD, pharmacology
phorbol 13 acetate 12 myristate: PD, pharmacology
daidzein: PD, pharmacology
hexamethylenebisacetamide: PD, pharmacology

L109 ANSWER 55 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
94208786 EMBASE Urinary lignan and isoflavonoid excretion in premenopausal women consuming flaxseed powder. Lampe J.W.; Martini M.C.; Kurzer M.S.; Adlercreutz H.; Slavin J.L.. Department of Food Science/Nutrition, University of Minnesota, 1334 Eckles Avenue, St Paul, MN 55108, United States. AM. J. CLIN. NUTR. 60/1 (122-128) 1994. ISSN: 0002-9165. CODEN: AJCNAC. Pub. Country: United States. Language: English. Summary Language: English.

AB Lignans and isoflavonoid phytoestrogens, produced from plant precursors by colonic bacteria, may protect against certain cancers. We examined the effects of flaxseed consumption on urinary lignans and isoflavonoids. Eighteen women consumed their usual omnivorous diets for three menstrual cycles and their usual diets supplemented with flaxseed powder (10 g/d) for three cycles in a randomized crossover design. Three-day urine samples from follicular and luteal phases were analyzed for lignans and isoflavonoids by isotope-dilution gas chromatography-mass spectrometry. Excretion of the lignans enterodiol and enterolactone increased with flaxseed from 1.09 .+-. 1.08 and 3.16 .+-. 1.47 to 19.48 .+-. 1.10 and 27.79 .+-. 1.50 .mu.mol/d, respectively ($P < 0.0002$). Enterodiol and enterolactone excretion varied among subjects in response to flaxseed (3- to 285-fold increase). There were no differences in excretion of isoflavonoids (daidzein, genistein, equol, and O-desmethylangolensin) or the lignan matairesinol with flaxseed. Excretion was not altered by phase of menstrual cycle or duration of flaxseed consumption.

CT EMTAGS: therapy (0160); mammal (0738); human (0888); female (0042); clinical article (0152); controlled study (0197); adult (0018); article (0060)
Medical Descriptors:
***diet supplementation**

*urinary excretion
***menstrual cycle**
isotope dilution assay
gas chromatography
mass spectrometry
follicular phase
luteal phase
human
female
clinical article
controlled study
adult
article
Drug Descriptors:
*powder
linseed
*linseed oil
*lignan: EC, endogenous compound
*isoflavonoid: EC, endogenous compound
enterolactone: EC, endogenous compound
daidzein: EC, endogenous compound
genistein: EC, endogenous compound
matairesinol: EC, endogenous compound
unclassified drug
enterodiol: EC, endogenous compound
equol: EC, endogenous compound
2 desmethylangolensin: EC, endogenous compound

L109 ANSWER 56 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
95088356 EMBASE The inducible form of nitric oxide synthase (iNOS) in insulin-producing cells. Eizirik D.L.; Leijerstam F.. Department of Medical Cell Biology, Uppsala University, Biomedicum, Box 571, S-751 23 Uppsala, Sweden. Diabete et Metabolisme 20/2 (116-122) 1994. ISSN: 0338-1684. CODEN: DIMEDU. Pub. Country: France. Language: English. Summary Language: English; French.

AB The enzyme nitric oxide synthase catalyzes the conversion of L-arginine to citrulline and the radical nitric oxide, a short-lived mediator which can be produced in a variety of cell types. Overproduction of nitric oxide is probably implicated in the pathogenesis of several immunologically mediated diseases, including insulin-dependent diabetes mellitus (Type 1). Insulin-producing cells exposed to cytokines, especially interleukin-1, express an inducible form of nitric oxide synthase which is similar to that observed in activated macrophages. Induction of this enzyme mRNA in these cells depends on protein synthesis, and it is probably modulated by protein products of early response genes, such as C-fos. Cytokines seem to activate .beta.-cell inducible-nitric oxide synthase mostly by stimulating mRNA transcription, but drugs such as nicotinamide and dexamethasone inhibit interleukin 1 induced nitric oxide production by posttranscriptional mechanisms. Considering the potential role for nitric oxide in .beta.-cell damage during the early stages of Type 1 diabetes, it is of high relevance to further characterize the regulation of this enzyme in insulin-producing cells.

CT EMTAGS: digestive system (0935); pancreas (0939); mammal (0738); human (0888); nonhuman (0777); conference paper (0061); enzyme (0990)
Medical Descriptors:
*pancreas cell
human
nonhuman
conference paper
Drug Descriptors:
*insulin: EC, endogenous compound
*nitric oxide synthase: EC, endogenous compound
***nicotinamide: PD, pharmacology**
*dexamethasone: PD, pharmacology
*cytokine: PD, pharmacology
***genistein: PD, pharmacology**

interleukin 4: PD, pharmacology
interleukin 10: PD, pharmacology
trifluoperazine: PD, pharmacology
gamma interferon: PD, pharmacology
aminoguanidine: PD, pharmacology
interleukin 1: PD, pharmacology
phorbol 13 acetate 12 myristate: PD, pharmacology
interleukin 1beta: PD, pharmacology
tumor necrosis factor alpha: PD, pharmacology
n(g) nitroarginine: PD, pharmacology
n(g) nitroarginine methyl ester: PD, pharmacology

L109 ANSWER 57 OF 79 MEDLINE DUPLICATE 4
94336429 Soy intake and cancer risk: a review of the in vitro and in vivo data. Messina M J; Persky V; Setchell K D; Barnes S. (National Cancer Institute, National Institutes of Health, Bethesda, MD..)NUTRITION AND CANCER, (1994) 21 (2) 113-31. Ref: 112. Journal code: O94. ISSN: 0163-5581. Pub. country: United States. Language: English.

AB International variations in cancer rates have been attributed, at least in part, to differences in dietary intake. Recently, it has been suggested that consumption of soyfoods may contribute to the relatively low rates of breast, colon, and prostate cancers in countries such as China and Japan. Soybeans contain a number of anticarcinogens, and a recent National Cancer Institute workshop recommended that the role of soyfoods in cancer prevention be investigated. In this review, the hypothesis that soy intake reduces cancer risk is considered by examining relevant in vitro, animal, and epidemiological data. Soybeans are a unique dietary source of the isoflavone genistein, which possesses weak estrogenic activity and has been shown to act in animal models as an antiestrogen. Genistein is also a specific inhibitor of protein tyrosine kinases; it also inhibits DNA topoisomerases and other critical enzymes involved in signal transduction. In vitro, genistein suppresses the growth of a wide range of cancer cells, with IC50 values ranging from 5 to 40 microM (1-10 micrograms/ml). Of the 26 animal studies of experimental carcinogenesis in which diets containing soy or soybean isoflavones were employed, 17 (65%) reported protective effects. No studies reported soy intake increased tumor development. The epidemiological data are also inconsistent, although consumption of nonfermented soy products, such as soymilk and tofu, tended to be either protective or not associated with cancer risk; however, no consistent pattern was evident with the fermented soy products, such as miso. Protective effects were observed for both hormone- and nonhormone-related cancers. While a definitive statement that soy reduces cancer risk cannot be made at this time, there is sufficient evidence of a protective effect to warrant continued investigation.

CT Check Tags: Animal; Human
*Isoflavones: PD, pharmacology
Neoplasms: EP, epidemiology
***Neoplasms: PC, prevention & control**
Neoplasms, Experimental: PC, prevention & control
Protein-Tyrosine Kinase: AI, antagonists & inhibitors
Risk Factors
Signal Transduction: DE, drug effects
***Soybeans**
Tumor Cells, Cultured

L109 ANSWER 58 OF 79 MEDLINE
95042274 Reversion of the transformed phenotypes of v-H-ras NIH3T3 cells by flavonoids through attenuating the content of phosphotyrosine. Kuo M L; Lin J K; Huang T S; Yang N C. (Institute of Toxicology, College of Medicine, National Taiwan University, Taipei, R.O.C..)CANCER LETTERS, (1994 Nov 25) 87 (1) 91-7. Journal code: CMX. ISSN: 0304-3835. Pub. country: Ireland. Language: English.

AB Fifteen flavonoids were employed to examine their effects on the morphological changes, foci formation in soft agar and cellular growth in v-H-ras-transformed NIH3T3 cells. The data presented here demonstrated that only three specific flavonoids--apigenin,

kaempferol, and genistein--exhibited the reverting effect on the transformed phenotypes of ras-3T3 cells. For example, treatment with 25 microM of these flavonoids could effectively reverse the transformed morphology of ras-3T3 cells into flatter cells with contact inhibition. Colony formation in soft agar was decreased to 0.11%, 0.15%, and 0.35% by 25 microM apigenin, kaempferol, and genistein, respectively, as compared with control (0.92%). It was also found that the proliferation of ras-3T3 cells was significantly inhibited by these compounds in a dose-dependent manner. Finally, two biochemical parameters, the content of phosphotyrosine and cAMP, were examined to see whether affected by these compounds. The results showed the phosphotyrosine content in ras-3T3 cells was dramatically decreased by apigenin and kaempferol, but that was slightly reduced by genistein. By contrast, these three flavonoids all failed to significantly alter the level of cAMP within this transformant. Based on these observations, we suggest that some specific flavonoids are capable of reverting the transforming properties of v-H-ras transformed cells. The possible mechanism of this reversion is not mediated by activating the protein kinase A or its associated pathways, but rather inhibiting tyrosine kinases, subsequently leading to the blockage of p21ras-mediated signal transduction circuitry.

CT Check Tags: Animal; Support, Non-U.S. Gov't
*Bioflavonoids: PD, pharmacology
Cell Division: DE, drug effects
Cell Line, Transformed
***Cell Transformation, Neoplastic: DE, drug effects**
*Cell Transformation, Viral: DE, drug effects
Culture Media
Cyclic AMP: ME, metabolism
Dose-Response Relationship, Drug
Flavones: PD, pharmacology
*Genes, ras
Isoflavones: PD, pharmacology
Mice
Oils, Volatile: PD, pharmacology
Phenotype
Protein-Tyrosine Kinase: AI, antagonists & inhibitors
Quercetin: AA, analogs & derivatives
Quercetin: PD, pharmacology
*Tyrosine: AA, analogs & derivatives
Tyrosine: ME, metabolism
3T3 Cells

L109 ANSWER 59 OF 79 MEDLINE
94048652 Plasma concentrations of phyto-oestrogens in Japanese men. Adlercreutz H; Markkanen H; Watanabe S. (Department of Clinical Chemistry, University of Helsinki, Mellahti Hospital, Finland..)LANCET, (1993 Nov 13) 342 (8881) 1209-10. Journal code: L0S. ISSN: 0140-6736. Pub. country: ENGLAND: United Kingdom. Language: English.

AB A low mortality from prostatic cancer is found in Japanese men consuming a low-fat diet with high content of soy products, a rich source of isoflavonoids. We therefore assayed four isoflavonoids in plasma of 14 Japanese and 14 Finnish men. The geometric mean plasma total individual isoflavonoid levels were 7 to 110 times higher in the Japanese than in the Finnish men. Genistein, a tyrosine kinase inhibitor, occurred in the highest concentration (geometric mean 276 nmol/L). We hypothesise that these high phyto-oestrogen levels may inhibit the growth of prostatic cancer in Japanese men, which may explain the low mortality from prostatic cancer in that country.

CT Check Tags: Comparative Study; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Chromans: BL, blood
Diet
*Estrogens, Non-Steroidal: BL, blood
Finland
*Isoflavones: BL, blood
Japan
Middle Age

Prostatic Neoplasms: ET, etiology
Prostatic Neoplasms: MO, mortality
Prostatic Neoplasms: PC, prevention & control
Risk Factors

L109 ANSWER 60 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
94115391 EMBASE Assessment of the estrogenic activity of phytoestrogens isolated from bourbon and beer. Rosenblum E.R.; Stauber R.E.; Van Thiel D.H.; Campbell I.M.; Gavaler J.S.. Baptist Medical Center, Oklahoma Transplant Institute, 3300 Northwest Expressway, Oklahoma City, OK 73112, United States. ALCOHOL. CLIN. EXP. RES. 17/6 (1207-1209) 1993. ISSN: 0145-6008. CODEN: ACRSDM. Pub. Country: United States. Language: English. Summary Language: English.

AB Phytoestrogenic substances have previously been isolated and identified in two alcoholic beverages: bourbon and beer. To delineate the relative potencies of the estrogenic substances of plant origin thus far identified in these commonly consumed alcoholic beverages, we evaluated the ability of biochanin A, .beta.-sitosterol, genistein, and daidzein to bind to cytosolic estrogen receptor binding sites. The in vitro studies demonstrated that each of the contained substances was capable of effectively competing for cytosolic estrogen receptor binding sites of rat liver and uterus. Further, the two phytoestrogenic constituents of bourbon, .beta.-sitosterol and biochanin A, were less potent than those present in beer. Given the high concentration of .beta.-sitosterol in bourbon, we chose to evaluate the estrogenicity of .beta.- sitosterol in vivo using ovariectomized rats. .beta.-sitosterol was administered either daily or intermittently at 3 doses, based on amounts previously determined to be present in bourbon. The in vivo studies demonstrated that .beta.-sitosterol is capable of producing a weak estrogenic effect only at the lowest dose (6.2 .mu.g/dl) administered intermittently. These responses suggest that .beta.-sitosterol may be weakly estrogenic at low doses, but is unable to maintain such an effect at higher doses.

CT EMTAGS: etiology (0135); nonhuman (0777); male (0041); female (0042); animal model (0106); biological model (0502); controlled study (0197); oral drug administration (0181); priority journal (0007); article (0060); therapy (0160)
Medical Descriptors:
***alcohol consumption**
*estrogen activity
***beer**
alcohol liver cirrhosis: ET, etiology
feminization: ET, etiology
ovariectomy
estrogen receptor
receptor binding
binding site
hormone receptor interaction
dose response
nonhuman
male
female
animal model
controlled study
oral drug administration
priority journal
article
Drug Descriptors:
*alcohol: TO, drug toxicity
*plant extract: AD, drug administration
*plant extract: CM, drug comparison
*plant extract: DO, drug dose
*plant extract: IT, drug interaction
*plant extract: PD, pharmacology
*sitosterol: AD, drug administration
*sitosterol: CM, drug comparison
*sitosterol: DO, drug dose
*sitosterol: IT, drug interaction

*sitosterol: PD, pharmacology
***biochanin a: AD, drug administration**
***biochanin a: CM, drug comparison**
***biochanin a: DO, drug dose**
***biochanin a: IT, drug interaction**
***biochanin a: PD, pharmacology**
genistein

L109 ANSWER 61 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
94209391 EMBASE Differentiation of human myeloblastic leukemia ML-1 cells into macrophages by staurosporine, an inhibitor of protein kinase activities. Makishima M.; Honma Y.; Hozumi M.; Sampi K.; Motoyoshi K.; Nagata N.; Hattori M.. Department of Chemotherapy, Saitama Cancer Research Institute, Ina-machi, Saitama 362, Japan. EXP. HEMATOL. 21/7 (839-845) 1993. ISSN: 0301-472X. CODEN: EXHEBH. Pub. Country: United States. Language: English. Summary Language: English.

AB Protein kinase activities are involved in cellular proliferation and differentiation, and inhibitors of these activities are useful for studying the mechanisms of induction of differentiation. We found that staurosporine, an inhibitor of protein kinase activities, induced morphological differentiation of human myeloblastic leukemia ML-1 cells along myelomonocytic lineage and also induced functional differentiation (increase in nitroblue tetrazolium-reducing and lysozyme activities? in the cells. Several other protein kinase inhibitors such as 1-(5-isoquinolinesulfonyl)-2-methylpiperazine dihydrochloride (H-7), sphingosine, N-(6-aminoethyl)-5-chloro-1-naphthalenesulfonamide and 1-(5-chloronaphthalene-1-sulfonyl)-1H-hexahydro-1,4-diazepine hydrochloride (ML-9) did not induce the differentiation of ML-1 cells. Treatment with staurosporine induced formation of granules in ML-1 cells, and the granules showed metachromasia by toluidine blue staining; however, histamine content did not increase. The 'metachromatic' ML-1 cells were positive for CD14, indicating that staurosporine induced the differentiation of ML-1 cells into metachromatic monocytes/macrophages. 1.alpha.,25-dihydroxyvitamin D3 (VD3) enhanced appearance of metachromatic granules in staurosporine-treated cells. These results suggest that modulation of protein phosphorylation by a staurosporine-sensitive protein kinase(s) may be associated with differentiation of ML-1 leukemia cells.

CT EMTAGS: malignant neoplastic disease (0306); therapy (0160); blood and hemopoietic system (0927); reticuloendothelial system (0924); mammal (0738); human (0888); controlled study (0197); priority journal (0007); article (0060)
Medical Descriptors:
*myeloid leukemia: DT, drug therapy
*cell differentiation
myeloblast
macrophage
human
controlled study
priority journal
article
Drug Descriptors:
*staurosporine: PD, pharmacology
*protein kinase inhibitor: PD, pharmacology
1 (5 isoquinolinesulfonyl) 2 methylpiperazine: PD, pharmacology
1 (5 chloro 1 naphthalenesulfonyl)hexahydro 1h 1,4 diazepine: PD, pharmacology
sphingosine: PD, pharmacology
genistein: PD, pharmacology
calcitriol: PD, pharmacology
retinoic acid: PD, pharmacology
recombinant interleukin 5: PD, pharmacology
recombinant granulocyte macrophage colony stimulating factor: PD, pharmacology
unclassified drug
a 3: PD, pharmacology
recombinant macrophage colony stimulating factor: PD, pharmacology

L109 ANSWER 62 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
93238905 EMBASE Hormone induction of luteinization and prostaglandin endoperoxide synthase-2 involves multiple cellular signaling pathways. Morris J.K.; Richards J.S.. Department of Cell Biology, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030, United States. ENDOCRINOLOGY 133/2 (770-779) 1993. ISSN: 0013-7227. CODEN: ENDOAO. Pub. Country: United States. Language: English. Summary Language: English.

AB To determine the cellular signaling pathways involved in granulosa cell luteinization, known activators of protein kinase-A (LH and FSH) and protein kinase-C [GnRH and phorbol 12-myristate 13-acetate (PMA)] as well as inhibitors of tyrosine kinases (AG18 and genistein) were tested in an in vitro system using specific markers of luteinization (cell hypertrophy, side- chain cleavage cytochrome P450, and progesterone) and ovulation [prostaglandin endoperoxide synthase-2 (PGS-2)]. When preovulatory follicles were incubated in the presence of an ovulatory (500 ng/ml) dose of LH or high GnRH (1 .mu.M), the granulosa cells harvested from these follicles assumed and maintained a stable luteal cell phenotype in vitro. Granulosa cells harvested from follicles incubated in subovulatory doses of LH (5 and 50 ng/ml), lower doses of GnRH (5, 50, and 500 nM), or PMA alone were unable to form a stable luteal cell phenotype. When PMA was combined with subovulatory doses of LH, granulosa cells luteinized, and PGS-2 protein was induced. AG18 (or genistein) blocked agonist induction of luteinization and of PGS-2 mRNA and protein when present during the first 2 h (0-2 h) of follicle incubation, but failed to block these events if added for the last 2 h (5-7 h of incubation). Combined, these results provide evidence to support a primary role for cAMP and protein kinase-A, a supportive but essential role for protein kinase-C, and an obligatory role for tyrosine kinases acting at an early stage in the cascade of events required for luteinization and ovulation.

CT EMTAGS: female genital system (0957); endocrine system (0970); nonhuman (0777); female (0042); rat (0733); mammal (0738); animal experiment (0112); controlled study (0197); animal tissue, cells or cell components (0105); adolescent (0017); priority journal (0007); article (0060); enzyme (0990)
Medical Descriptors:
***luteinization**
signal transduction
granulosa cell
ovary follicle
ovulation
nonhuman
female
rat
animal experiment
controlled study
animal cell
adolescent
priority journal
article
Drug Descriptors:
*prostaglandin synthase: EC, endogenous compound
protein kinase c: EC, endogenous compound
cyclic amp dependent protein kinase: EC, endogenous compound
gonadorelin
phorbol 13 acetate 12 myristate
genistein
luteinizing hormone: EC, endogenous compound

L109 ANSWER 63 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
93272596 EMBASE Effects of the protein phosphorylation inhibitor genistein on maturation of pig oocytes in vitro. Jung T.; Fulka J. Jr.; Lee C.; Moor R.M.. Department of Molecular Embryology, Inst. Animal Physiology and Genetics, Babraham, Cambridge CB2 4AT, United Kingdom. J. REPROD. FERTIL. 98/2 (529-535) 1993. ISSN: 0022-4251. CODEN: JRPFA4. Pub. Country: United Kingdom. Language: English.

Summary Language: English.

AB In vitro maturation of cumulus enclosed and denuded pig oocytes was reversibly inhibited by the protein kinase inhibitor genistein. The half-maximal effect on maturation was observed at 40 .mu.g ml-1. Genistein inhibited total protein phosphorylation and synthesis with the same dose-response relationship (ED50: 40 .mu.g ml-1). Protein phosphorylation and synthesis patterns were changed by effective concentrations of genistein. Pig oocytes were sensitive to genistein during the first 12 h of in vitro maturation. This genistein sensitive period corresponds closely with the period of sensitivity to the protein synthesis inhibitor cycloheximide. Whereas the inhibition of protein synthesis affects only nuclear membrane breakdown and not chromatin condensation, genistein inhibits both events. The results of these experiments suggest that protein phosphorylation and synthesis play major roles during pig oocyte maturation in vitro. It is concluded that genistein inhibited protein phosphorylation is a regulator of chromatin condensation, whereas both new protein synthesis and phosphorylation appear to be required for nuclear membrane disassembly. Caution about this second conclusion is, however, necessary because of the dual action of genistein on both protein phosphorylation and indirectly on protein synthesis.

CT EMTAGS: chemical procedures (0107); nonhuman (0777); female (0042); animal tissue, cells or cell components (0105); priority journal (0007); article (0060)

Medical Descriptors:
***oocyte maturation**
*protein synthesis inhibition
protein phosphorylation
dose response
protein synthesis
cell nucleus membrane
chromatin
nonhuman
female
animal tissue
priority journal
article

Drug Descriptors:
***genistein**
protein kinase inhibitor
cycloheximide

L109 ANSWER 64 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.

93332785 EMBASE Maturation-dependent regulation of protein kinase C activity by vitamin D3 metabolites in chondrocyte cultures. Sylvia V.L.; Schwartz Z.; Schuman L.; Morgan R.T.; Mackey S.; Gomez R.; Boyan B.D.. Department of Orthopaedics, Univ. of Texas Health Science Center, San Antonio, TX 78284, United States. J. CELL. PHYSIOL. 157/2 (271-278) 1993. ISSN: 0021-9541. CODEN: JCLLAX. Pub. Country: United States. Language: English. Summary Language: English.

AB Vitamin D3 metabolites regulate the differentiation of chondrocytes isolated from the growth zone or resting zone of rat costochondral cartilage. Since some of the direct membrane effects of vitamin D metabolites are nongenomic, we hypothesized that protein kinase C (PKC) plays a role in signal transduction for these chondrocyte differentiation factors and that the regulation of PKC by the vitamin D metabolites is cell maturation dependent. Confluent, fourth passage cultures of growth zone and resting zone chondrocytes were treated with vitamin D3 metabolites for up to 24 h, lysed, and cell extracts assayed for kinase activity using a specific PKC substrate peptide. The addition of 1,25-(OH)2D3 to growth zone cell cultures resulted in a rapid dose-dependent stimulation of PKC, significant at 10-9-10-7 M, beginning at 3 min and sustained until 90 min; 1,25-(OH)2D3 had no effect on PKC activity in resting zone chondrocyte cultures. The addition of 24,25-(OH)2D3 to resting zone cultures showed a slower PKC activation, with significant stimulation seen at 90-360 min for 10-8-10-7 M 24,25-(OH)2D3.

However, 24,25-(OH)2D3 had no effect on PKC activity in growth zone cell cultures at all times and concentrations examined. The specificity of PKC stimulation by the vitamin D3 metabolites was verified using a specific pseudosubstrate region peptide inhibitor, which reduced PKC activity when included in the reaction mixture. Pretreatment of the cultures with U73,122, a phospholipase C inhibitor, decreased 1,25-(OH)2D3-stimulated PKC activity but had no effect upon 24,25-(OH)2D3-induced activity. The tyrosine kinase inhibitor, genistein, did not inhibit the PKC response in either vitamin D3 metabolites-treated culture. Neither actinomycin D nor cycloheximide affected 1,25-(OH)2D3-induced PKC activity in growth zone chondrocyte cultures, while both compounds inhibited 24,25-(OH)2D3-induced activity in resting zone chondrocyte cultures. The results of this study indicate that vitamin D metabolites stimulate PKC activity in a metabolite- and cell-maturation-specific manner. Effects of 1,25-(OH)2D3 appear to be nongenomic, whereas the effects of 24,25-(OH)2D3 probably involve a genomic mechanism.

CT EMTAGS: nonhuman (0777); rat (0733); mammal (0738); controlled study (0197); animal tissue, cells or cell components (0105); priority journal (0007); article (0060); enzyme (0990)
Medical Descriptors:
*cell differentiation
cartilage cell
enzyme regulation
maturation
nonhuman
rat
controlled study
animal cell
priority journal
article
chondrogenesis
Drug Descriptors:
*protein kinase c: EC, endogenous compound
***colecalciferol: PD, pharmacology**
***colecalciferol: DO, drug dose**
*protein tyrosine kinase: EC, endogenous compound
***calcitriol: PD, pharmacology**
***calcitriol: DO, drug dose**
***24,25 dihydroxycolecalciferol: PD, pharmacology**
***24,25 dihydroxycolecalciferol: DO, drug dose**
genistein: PD, pharmacology
enzyme inhibitor: PD, pharmacology
dactinomycin: PD, pharmacology
cycloheximide: PD, pharmacology

L109 ANSWER 65 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
93174208 EMBASE Antimutagenic effects of flavonoids, chalcones and structurally related compounds on the activity of 2-amino-3-methylimidazo[4,5-f]quinoline (IQ) and other heterocyclic amine mutagens from cooked food. Edenharder R.; Von Petersdorff I.; Rauscher R.. Institute of Hygiene, University of Mainz, Augustusplatz, D-6500 Mainz, Germany, Federal Republic of. MUTAT. RES. FUNDAM. MOL. MECH. MUTAGEN. 287/2 (261-274) 1993. ISSN: 0027-5107. CODEN: MRFMEC. Pub. Country: Netherlands. Language: English. Summary Language: English.

AB Sixty-four flavonoids were tested for their antimutagenic potencies with respect to IQ in Salmonella typhimurium TA98 and in part also towards MeIQ, MeIQx, Trp-P-2, and Glu-P-1 and in S. typhimurium TA100. Antimutagenic potencies were quantified by the inhibitory dose for 50% reduction of mutagenic activity (ID50). A carbonyl function at C-4 of the flavane nucleus seems to be essential for antimutagenicity: two flavanols and four anthocyanidines were inactive. Again, five isoflavons, except biochanin A, were inactive. Within the other groups of 21 flavones, 16 flavonols and 16 flavanones the parent compounds flavone, flavonol, and flavanone possessed the highest antimutagenic potencies (ID50: 4.1, 2.5, 5.5 nmoles). Increasing polarity by introduction of hydroxyl functions reduced antimutagenic potency. Reducing polarity of hydroxy

flavonoids by methyl etherification, however, increased antimutagenic potency again. 6-Hydroxy- and 2'-hydroxy substituted flavonoids were considerably less potent antimutagens. Of 11 flavonoid glycosides tested all compounds except apigenin- and luteolin-7-glucoside (ID50: 74, 115 nmoles) were inactive or only weakly antimutagenic. Rings C and A of the nucleus were not essential for antimutagenicity: chalcone and three derivatives were nearly as active as comparable flavones while antimutagenicity of benzylidenacetone was considerably reduced (ID50: 95 nmoles). Cinnamylaldehyde and cinnamoates, however, were inactive. A planar structure in the vicinity of the carbonyl group may also be important for antimutagenicity. Flavanones were less potent antimutagens than the corresponding flavones, but dihydrochalcones and 14 structurally related saturated aromatic carbonyl compounds were inactive. Fisetin and 6-hydroxyflavone were competitive inhibitors, but luteolin was a mixed type inhibitor. The inhibition mechanisms of flavone, kaempferol, morin, flavanone, and 2'-hydroxyflavanone were concentration dependent, being competitive at low concentrations and mixed or non-competitive (2'-hydroxyflavanone) at concentrations about the ID50 value. No fundamental differences between the two tester strains and no clear influence of mutagen structure on antimutagenic potency could be detected.

CT EMTAGS: heredity (0137); bacterium (0762); nonhuman (0777); controlled study (0197); priority journal (0007); article (0060); therapy (0160)

Medical Descriptors:
*mutagenicity
*mutation rate
***food**
*cooking
salmonella typhimurium
structure activity relation
nonhuman
controlled study
priority journal
article

Drug Descriptors:
*flavonoid: PD, pharmacology
*flavonoid: DO, drug dose
*flavonoid: CM, drug comparison
*flavonoid: DV, drug development
*chalcone derivative: PD, pharmacology
*chalcone derivative: DO, drug dose
*chalcone derivative: CM, drug comparison
*chalcone derivative: DV, drug development
fisetin: PD, pharmacology
fisetin: DO, drug dose
fisetin: CM, drug comparison
kaempferol: PD, pharmacology
kaempferol: DO, drug dose
kaempferol: CM, drug comparison
luteolin: PD, pharmacology
luteolin: DO, drug dose
luteolin: CM, drug comparison
flavone: PD, pharmacology
flavone: DO, drug dose
flavone: CM, drug comparison
flavanone: PD, pharmacology
flavanone: DO, drug dose
flavanone: CM, drug comparison
apigenin: PD, pharmacology
apigenin: DO, drug dose
apigenin: CM, drug comparison
luteolin 7 glucoside: PD, pharmacology
luteolin 7 glucoside: DO, drug dose
luteolin 7 glucoside: CM, drug comparison
6 hydroxyflavone: PD, pharmacology
6 hydroxyflavone: DO, drug dose

6 hydroxyflavone: CM, drug comparison
morin: PD, pharmacology
morin: DO, drug dose
morin: CM, drug comparison
chalcone: PD, pharmacology
chalcone: DO, drug dose
chalcone: CM, drug comparison
biochanin a: PD, pharmacology
biochanin a: DO, drug dose
biochanin a: CM, drug comparison
naringenin: PD, pharmacology
naringenin: DO, drug dose
naringenin: CM, drug comparison
hesperetin: PD, pharmacology
hesperetin: DO, drug dose
hesperetin: CM, drug comparison
3 hydroxyflavone: PD, pharmacology
3 hydroxyflavone: DO, drug dose
3 hydroxyflavone: CM, drug comparison
unclassified drug
antimutagenic agent: PD, pharmacology
antimutagenic agent: DO, drug dose
antimutagenic agent: CM, drug comparison
antimutagenic agent: DV, drug development
flavanole: PD, pharmacology
flavanole: DO, drug dose
flavanole: CM, drug comparison
2' hydroxyflavanone: PD, pharmacology
2' hydroxyflavanone: DO, drug dose
2' hydroxyflavanone: CM, drug comparison
baicalein: TO, drug toxicity
baicalein: PD, pharmacology
baicalein: DO, drug dose
baicalein: CM, drug comparison

L109 ANSWER 66 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
93252941 EMBASE Lung tumors in strain A mice: Application for studies in cancer chemoprevention. Stoner G.D.; Adam-Rodwell G.; Morse M.A.. Ohio State University, Department of Preventive Medicine, Arthur G. James Cancer Hospital, 300 West 10th Avenue, Columbus, OH 43210, United States. J. CELL. BIOCHEM. 52/SUPPL. 17 F (95-103) 1993. ISSN: 0730-2312. CODEN: JCEBD5. Pub. Country: United States. Language: English. Summary Language: English.

AB Strain A mice develop a high incidence of spontaneous lung tumors during their lifetime. These tumors may be found in some animals as early as 3 to 4 weeks of age, increasing to nearly 100% by 24 months of age. The strain A mouse is also highly susceptible to the induction of lung tumors by several classes of chemical carcinogens and has been used extensively as a mouse lung tumor bioassay for assessing the carcinogenic activity of a variety of chemicals. In addition to its use in carcinogen detection, the strain A mouse lung tumor model has been employed extensively for the identification of inhibitors of chemical carcinogenesis. A number of chemopreventive agents including .beta.-naphthoflavone, butylated hydroxyanisole, ellagic acid, phenethyl isothiocyanate, phenylpropyl isothiocyanate, phenylbutyl isothiocyanate, phenylhexyl isothiocyanate, indole-3-carbinol, etc., have been shown to inhibit chemically induced lung tumors in strain A mice. In most instances, inhibition of lung tumorigenesis has been correlated with effects of the chemopreventive agent on the metabolic activation and/or detoxification of carcinogens. To date, no chemopreventive agent has been shown to inhibit lung tumorigenesis in strain A mice when administered after the carcinogen, i.e., during the promotion/progression stages of tumor development. Efforts should be made to develop a standardized protocol in strain A mice for evaluating chemopreventive agents as inhibitors of both the initiation and progression stages of lung tumor development.

CT EMTAGS: **malignant neoplastic disease** (0306); prevention (0165); therapy (0160); nonhuman (0777); mouse (0727); mammal

(0738); animal model (0106); biological model (0502); oral drug administration (0181); priority journal (0007); conference paper (0061)
Medical Descriptors:
***cancer: PC, prevention**
***cancer: DT, drug therapy**
*chemoprophylaxis
***lung tumor**
diet
tea
nonhuman
mouse
animal model
oral drug administration
priority journal
conference paper
Drug Descriptors:
*isothiocyanic acid: PD, pharmacology
*isothiocyanic acid: DT, drug therapy
*isothiocyanic acid: CM, drug comparison
*benzo[a]pyrene: TO, drug toxicity
beta naphthoflavone: PD, pharmacology
butylated hydroxyanisole: PD, pharmacology
ethoxyquin: PD, pharmacology
sodium cyanate: PD, pharmacology
ellagic acid: PD, pharmacology
sulindac: PD, pharmacology
biochanin a: PD, pharmacology
plant extract: PD, pharmacology
3 indolemethanol: PD, pharmacology
limonene: PD, pharmacology
citrus oil: PD, pharmacology
citrus oil: DT, drug therapy
unclassified drug
chemopreventive agent: PD, pharmacology
chemopreventive agent: DT, drug therapy
chemopreventive agent: CM, drug comparison
chemopreventive agent: DV, drug development
tannin: PD, pharmacology
phenethyl isothiocyanate: PD, pharmacology
phenethyl isothiocyanate: DT, drug therapy
phenethyl isothiocyanate: CM, drug comparison
4 phenylbutyl isothiocyanate: PD, pharmacology
4 phenylbutyl isothiocyanate: DT, drug therapy
4 phenylbutyl isothiocyanate: CM, drug comparison
3 phenylpropyl isothiocyanate: PD, pharmacology
3 phenylpropyl isothiocyanate: DT, drug therapy
3 phenylpropyl isothiocyanate: CM, drug comparison
5 phenylpentyl isothiocyanate: PD, pharmacology
5 phenylpentyl isothiocyanate: DT, drug therapy
5 phenylpentyl isothiocyanate: CM, drug comparison
6 phenylhexylisothiocyanate: PD, pharmacology
6 phenylhexylisothiocyanate: DT, drug therapy
6 phenylhexylisothiocyanate: CM, drug comparison

L109 ANSWER 67 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
94046128 EMBASE Metabolites of dietary (soya) isoflavones in human urine. Kelly G.E.; Nelson C.; Waring M.A.; Joannou G.E.; Reeder A.Y.. Department of Surgery, University of Sydney, Sydney, NSW 2006, Australia. CLIN. CHIM. ACTA 223/1-2 (9-22) 1993. ISSN: 0009-8981. CODEN: CCATAR. Pub. Country: Netherlands. Language: English. Summary Language: English.
AB This study was undertaken to better understand the metabolic fate of dietary isoflavones in humans. Twelve volunteers were challenged with soya flour and urinary diphenol levels were then determined by gas chromatography (GC) and gas chromatography-mass spectrometry (GC-MS). The presence of previously described urinary diphenols was confirmed, i.e. the isoflavones, daidzein and genistein; the isoflavonoid metabolites, equol, dihydrodaidzein (Int-O-D),

O-desmethyl-angolensin (O-Dma); the lignan, enterolactone. Diphenols detected for the first time were the isoflavone, glycitein and five novel isoflavonoid metabolites which are tentatively identified as 6'- hydroxy-O-desmethylangolensin (6'OH-O-Dma), dihydrogenistein (Int-O-G), dehydro-O-desmethylangolensin (dehydro-O-Dma) and two isomers of tetrahydrodaidzein. Urinary excretion rates of the three isoflavones (daidzein, genistein, glycitein) over a 3-day period following soya challenge showed moderate variation (4x, 6x and 12x, respectively) between the 12 individuals suggesting some individual variabilities in ability to deconjugate and to absorb dietary isoflavones. However, urinary excretion rates of each of three major isoflavonoid metabolites (equol, O-Dma, 6'OH-O- Dma) showed more marked variation (922x, 17x, 15x, respectively); while some of this variability may reflect varying individual ability to ferment dietary isoflavones per se, an inverse relationship was found between urinary levels of equol and both O-Dma and 6'OH-O-Dma suggesting individual variability in the preferred metabolic pathways of dietary isoflavones.

CT EMTAGS: higher plant (0697); plant (0699); mammal (0738); human (0888); human experiment (0104); normal human (0800); male (0041); female (0042); adult (0018); priority journal (0007); article (0060); pharmacokinetics (0194)
Medical Descriptors:
***dietary intake**
urine
gas chromatography
mass spectrometry
diet
soybean
human
human experiment
normal human
male
female
adult
priority journal
article
Drug Descriptors:
*isoflavone derivative: PK, pharmacokinetics
*isoflavone derivative: CR, drug concentration
*isoflavone derivative: AN, drug analysis
***genistein: PK, pharmacokinetics**
***genistein: CR, drug concentration**
***genistein: AN, drug analysis**
***daidzein: PK, pharmacokinetics**
***daidzein: CR, drug concentration**
***daidzein: AN, drug analysis**
*drug metabolite: CR, drug concentration
*drug metabolite: AN, drug analysis
glycitein: PK, pharmacokinetics
glycitein: CR, drug concentration
glycitein: AN, drug analysis
unclassified drug

L109 ANSWER 68 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
93225376 EMBASE Inhibition of tumor promoter-induced hydrogen peroxide formation in vitro and in vivo by genistein. Wei H.; Wei L.; Frenkel K.; Bowen R.; Barnes S.. Environmental Health Sciences Dept., University of Alabama, Birmingham, AL 35294, United States. NUTR. CANCER 20/1 (1-12) 1993. ISSN: 0163-5581. CODEN: NUCADQ. Pub. Country: United States. Language: English. Summary Language: English.

AB Here we report that genistein, a soybean isoflavone, strongly inhibits tumor promoter-induced H2O2 formation both in vivo and in vitro. Genistein suppressed H2O2 production by 12-O-tetradecanoylphorbol-13-acetate- (TPA) stimulated human polymorphonuclear leukocytes (PMNs) and HL-60 cells in a dose-dependent manner over the concentration range 1-150 .mu.M. Human PMNs were more sensitive to the inhibitory effect of genistein

than HL-60 cells (50% inhibitory concentration 14.8 and 30.2 .mu.M, respectively). In addition, genistein moderately inhibited superoxide anion formation by HL-60 cells and scavenged exogenously added H2O2 under the same conditions as in cell culture. However, the H2O2-scavenging effect of genistein was about 50% lower than its inhibition of cell-derived H2O2 formation at all concentrations. In the CD-1 mouse skin model, genistein strongly inhibited TPA-induced oxidant formation, edema, and PMN infiltration in mouse skin. Inhibition of TPA-mediated H2O2 in vivo may result from decreased cell- derived H2O2 formation, scavenging of H2O2 produced, and/or suppression of PMN infiltration into the dermis. The antioxidant properties of genistein may be responsible for its anticarcinogenic effects, and the dietary availability of genistein makes it a promising candidate for the prevention of human cancers.

CT EMTAGS: etiology (0135); blood and hemopoietic system (0927); higher plant (0697); plant (0699); mammal (0738); human (0888); nonhuman (0777); female (0042); mouse (0727); normal human (0800); animal experiment (0112); animal model (0106); biological model (0502); controlled study (0197); human tissue, cells or cell components (0111); animal tissue, cells or cell components (0105); article (0060); enzyme (0990)
Medical Descriptors:
*tumor promotion
*antineoplastic activity
drug effect
neutrophil
cell line
skin inflammation
skin edema
dose response
cell infiltration
soybean
human
nonhuman
female
mouse
normal human
animal experiment
animal model
controlled study
human cell
animal tissue
article
Drug Descriptors:
***genistein: DO, drug dose**
***genistein: PD, pharmacology**
*hydrogen peroxide: EC, endogenous compound
*superoxide: EC, endogenous compound
*phorbol 13 acetate 12 myristate
scavenger
antioxidant
horseradish peroxidase
myeloperoxidase
dimethyl sulfoxide

L109 ANSWER 69 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
92131551 EMBASE Dietary phytoestrogens and cancer: In vitro and in vivo studies. Adlercreutz H.; Mousavi Y.; Clark J.; Hockerstedt K.; Hamalainen E.; Wahala K.; Makela T.; Hase T.. Department of Clinical Chemistry, University of Helsinki, SF-00290 Helsinki, Finland. J. STEROID BIOCHEM. MOL. BIOL. 41/3-8 (331-337) 1992. ISSN: 0960-0760. CODEN: JSBBEZ. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Thirty postmenopausal women (11 omnivores, 10 vegetarians and 9 apparently healthy women with surgically removed breast cancer) were investigated with regard to the association of their urinary excretion of estrogens, lignans and isoflavonoids (all diphenols) with plasma sex hormone binding globulin (SHBG). A statistically significant positive correlation between urinary total diphenol

excretion and plasma SHBG was found which remained statistically significant after elimination of the confounding effect of body mass determined by body mass index (BMI). Furthermore we found a statistically significant negative correlation between plasma SHBG and urinary excretion of 16.alpha.-hydroxyestrone and estriol which also remained significant after eliminating the effect of BMI. Furthermore we observed that enterolactone (Enl) stimulates the synthesis of SHBG by HepG2 liver cancer cells in culture acting synergistically with estradiol and at physiological concentrations. Enl was rapidly conjugated by the liver cells, mainly to its monosulfate. Several lignans and the isoflavonoids daidzein and equol were found to compete with estradiol for binding to the rat uterine type II estrogen binding site (the s.c. bioflavonoid receptor). It is suggested that lignans and isoflavonoids may affect uptake and metabolism of sex hormones by participating in the regulation of plasma SHBG levels and in this way influence their biological activity and that they may inhibit cancer cell growth like some flavonoids by competing with estradiol for the type II estrogen binding sites.

CT EMTAGS: therapy (0160); mammal (0738); human (0888); female (0042); clinical article (0152); priority journal (0007); conference paper (0061)

Medical Descriptors:
***vegetarian diet**
***breast cancer: TH, therapy**
*receptor binding
urinary excretion
human
female
clinical article
priority journal
conference paper
Drug Descriptors:
*estrogen: EC, endogenous compound
*lignan: PD, pharmacology
*lignan: DO, drug dose
*lignan: CM, drug comparison
*isoflavonoid: PD, pharmacology
*isoflavonoid: DO, drug dose
*isoflavonoid: CM, drug comparison
*sex hormone binding globulin: EC, endogenous compound
daidzein: PD, pharmacology
daidzein: DO, drug dose
daidzein: CM, drug comparison
formononetin: PD, pharmacology
formononetin: DO, drug dose
formononetin: CM, drug comparison
matairesinol: PD, pharmacology
matairesinol: DO, drug dose
matairesinol: CM, drug comparison
unclassified drug
enterolactone: PD, pharmacology
enterolactone: DO, drug dose
enterolactone: CM, drug comparison
equol: PD, pharmacology
equol: DO, drug dose
equol: CM, drug comparison
isolariciresinol: PD, pharmacology
isolariciresinol: DO, drug dose
isolariciresinol: CM, drug comparison
enterodiol: PD, pharmacology
enterodiol: DO, drug dose
enterodiol: CM, drug comparison

L109 ANSWER 70 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
92118834 EMBASE Identification in human urine of a natural growth inhibitor for cells derived from solid paediatric tumours.
Schweigerer L.; Christeleit K.; Fleischmann G.; Adlercreutz H.; Wahala K.; Hase T.; Schwab M.; Ludwig R.; Fotsis T.. Dept.

Oncology/Immunology, Children's University Hospital, Ruprecht-Karls-Universitat, 6900 Heidelberg, Germany, Federal Republic of. EUR. J. CLIN. INVEST. 22/4 I (260-264) 1992. ISSN: 0014-2972. CODEN: EJCIB8. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Partially purified urine of healthy human subjects contains several fractions able to inhibit the proliferation of cultured human neuroblastoma cells. One of the most active fractions was further analysed by gas chromatography-mass spectrometry and shown to contain genistein, a substance formed in the human body from precursors obtained by diet. Synthetic genistein was able to inhibit the proliferation of human neuroblastoma cells with a half-maximal effect at 5-10 .mu.mol l-1 concentrations. Genistein displayed similar potencies in inhibiting the proliferation of cells derived from various other solid pediatric tumours. Our results suggest that genistein is a natural antineoplastic agent present in diet and that it could be useful for the therapy of paediatric tumours.

CT EMTAGS: malignant neoplastic disease (0306); mammal (0738); human (0888); priority journal (0007); article (0060)
Medical Descriptors:
*childhood cancer
*growth inhibition
***diet**
neuroblastoma
antineoplastic activity
human
priority journal
article
Drug Descriptors:
***genistein: PD, pharmacology**

L109 ANSWER 71 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.

93026147 EMBASE Action of thrombin receptor polypeptide in gastric smooth muscle: Identification of a core pentapeptide retaining full thrombin-mimetic intrinsic activity. Hollenberg M.D.; Yang S.-G.; Laniyonu A.A.; Moore G.J.; Saifeddine M.. Pharmacology/Therapeutics Department, Faculty of Medicine, University of Calgary, Calgary, Alta. T2N 4N1, Canada. MOL. PHARMACOL. 42/2 (186-191) 1992. ISSN: 0026-895X. CODEN: MOPMA3. Pub. Country: United States. Language: English. Summary Language: English.

AB We have used a guinea pig gastric longitudinal (LM) smooth muscle bioassay system to evaluate the contractile activities of a previously described thrombin receptor-derived polypeptide, S42FLLRNPNDKYEPF55 (one-letter amino acid code) (TRP42-55) and of a series of peptides derived from this sequence. The contractile activities of the polypeptides were compared with the actions of thrombin. Shortened peptides of the sequences S42FLLRNPND50, S42FLLRN47, and S42FLLR46 (TRP42-46) all exhibited contractile activities that were equivalent to or greater than those of the parent polypeptide, TRP42-55. Both TRP42-55 and TRP42-46 mimicked the action of thrombin, in terms of two different signal transduction pathways that were activated either in the LM preparation or in the related but distinct gastric circular muscle assay. In the LM preparation, the peptide FSLLR also exhibited appreciable, but much reduced, activity. Minimal activity was exhibited in the LM by the sequence SFLLA, but the lysine-containing analogue S42FLLK46 was about one fifth as potent as TRP42-46. In contrast, the receptor-derived sequences S42FLL45, S42FL44-NH2, F43LLR46, and S42ALLR46, as well as arginine- containing polypeptides beginning with the SF motif, SFRG and SFRGHITR, were inactive in the LM bioassay system, at concentrations of .gtoreq.200 .mu.M, as either agonists or antagonists against TRP42-55. In addition to its actions in the LM and circular muscle preparations, the active pentapeptide, TRP42- 46, also exhibited thrombin-mimetic intrinsic activity in a rat aortic arterial ring relaxation bioassay, whereas the pentapeptide S42FLLA46 and the tetrapeptide S42FLL45 were inactive. We conclude that the intrinsic biological activity of the thrombin receptor-derived peptide resides in the pentapeptide TRP42-46 and that the phenylalanine and arginine

residues at positions 43 and 46 play key roles in the activity of this pentapeptide in smooth muscle systems.

CT EMTAGS: digestive system (0935); stomach (0938); musculoskeletal system (0960); muscle (0961); guinea pig (0717); mammal (0738); congenital disorder (0315); nonhuman (0777); male (0041); animal tissue, cells or cell components (0105); priority journal (0007); article (0060); enzyme (0990)
Medical Descriptors:
*stomach muscle
*intrinsic sympathomimetic activity
*receptor binding
signal transduction
bioassay
guinea pig
vascular ring
muscle contractility
spectroscopy
amino acid analysis
high performance liquid chromatography
structure activity relation
binding affinity
nonhuman
male
animal tissue
animal cell
priority journal
article
Drug Descriptors:
*thrombin: PD, pharmacology
*polypeptide: PD, pharmacology
*pentapeptide: PD, pharmacology
arginine
phenylalanine
indometacin: PD, pharmacology
genistein: PD, pharmacology
guanine nucleotide binding protein: EC, endogenous compound

L109 ANSWER 72 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
91346803 EMBASE Induction of in vitro differentiation of mouse embryonal carcinoma (F9) cells by inhibitors of topoisomerases.
Kondo K.; Tsuneizumi K.; Watanabe T.; Oishi M.. Institute of Applied Microbiology, University of Tokyo, Bunkyo-ku, Tokyo 113, Japan.
CANCER RES. 51/19 (5398-5404) 1991. ISSN: 0008-5472. CODEN: CNREA8. Pub. Country: United States. Language: English. Summary Language: English.

AB To investigate the possible involvement of topoisomerases in embryonal differentiation, we examined the effect of topoisomerase inhibitors on the in vitro differentiation of mouse embryonal carcinoma F9 cells. We found that camptothecin, teniposide (VM-26), or genistein, specific inhibitors of topoisomerases, induced morphological as well as biochemical changes (production of tissue plasminogen activator, synthesis of laminin, and disappearance of stage-specific embryonic antigen 1) specific to F9 cell differentiation. Since these changes were indistinguishable from those observed in F9 differentiation induced by retinoic acid (plus dibutyryl cyclic AMP), it was suggested that inhibition of cellular topoisomerase activities triggered F9 cell differentiation into parietal endoderm-like cells in the same manner as retinoic acid (plus dibutyryl cyclic AMP). Experiments using differentiation-resistant mutant F9 cell lines, however, indicated that the molecular cascade involved in topoisomerase inhibitor-induced differentiation involves different steps from those functioning in the retinoic acid-induced differentiation cascade.

CT EMTAGS: malignant neoplastic disease (0306); enzyme (0990); nonhuman (0777); mouse (0727); mammal (0738); animal model (0106); biological model (0502); animal tissue, cells or cell components (0105); priority journal (0007); article (0060); therapy (0160)
Medical Descriptors:
*embryonal carcinoma

*dna topoisomerase
nonhuman
mouse
animal model
animal cell
priority journal
article
Drug Descriptors:
*camptothecin: PD, pharmacology
*camptothecin: CM, drug comparison
*teniposide: PD, pharmacology
*teniposide: CM, drug comparison
***genistein: PD, pharmacology**
***genistein: CM, drug comparison**
***retinoic acid: PD, pharmacology**
***retinoic acid: CM, drug comparison**

L109 ANSWER 73 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
91300379 EMBASE Tetrahydroisoquinoline alkaloids mimic direct but not receptor-mediated inhibitory effects of estrogens and phytoestrogens on testicular endocrine function. Possible significance for Leydig cell insufficiency in alcohol addiction. Stammel W.; Thomas H.; Staib W.; Kuhn-Velten W.N.. Frauenklinik, Biochemische Endokrinologie, Heinrich-Heine-Universitat, Moorenstrasse 5, D-4000 Dusseldorf, Germany, Federal Republic of. LIFE SCI. 49/18 (1319-1329) 1991. ISSN: 0024-3205. CODEN: LIFSAK. Pub. Country: United States. Language: English.

AB Possible effects of various tetrahydroisoquinolines (TIQs) on rat testicular endocrine function were tested in vitro in order to prove whether these compounds, some of which have been claimed to accumulate in alcoholics, may be mediators of the development of Leydig cell insufficiency, a well-known side-effect of ethanol ingestion. TIQ effects on different levels of regulation of testis function were compared in vitro with estrogen effects, since both classes of compounds have structural similarities. Gonadotropin-stimulated testosterone production by testicular Leydig cells was inhibited by tetrahydropapaveroline and isosalsoline, the IC50 values (30 .mu.M) being comparable to those of estradiol (3.mu.M), 2-hydroxyestradiol (10 .mu.M), and the phytoestrogens, coumestrol (15 .mu.M) and genistein (7 .mu.M); salsolinol (85 .mu.M) and salsoline (240 .mu.M) were less effective, and salsolidine was ineffective. None of these TIQs interacted significantly with testicular estrogen receptor as analyzed by estradiol displacement. However, tetrahydropapaveroline, isosalsoline and salsolinol competitively inhibited (Ki 130-150 .mu.M) substrate binding to cytochrome P45OXVII, one key enzyme of androgen biosynthesis, with similar efficiency as the estrogens did (Ki 50-110 .mu.M); salsoline and salsolidine were again much less effective. Since the efficient TIQ concentrations in this system are identical with those reported to generate central-nervous effects, it is concluded that certain TIQs may amplify peripheral inhibitory effects of ethanol on testicular endocrine function by their interaction with at least one enzyme of the androgen biosynthetic pathway.

CT EMTAGS: therapy (0160); male genital system (0956); endocrine system (0970); nonhuman (0777); male (0041); rat (0733); mammal (0738); animal tissue, cells or cell components (0105); newborn (0013); infant (0014); child (0022); priority journal (0007); article (0060)
Medical Descriptors:
*endocrine function
*leydig cell
*alcoholism
alcohol consumption
estrogen receptor
drug binding
nonhuman
male
rat
animal cell
newborn

priority journal
article
Drug Descriptors:
isosalsoline: PD, pharmacology
isosalsoline: CM, drug comparison
unclassified drug
*tetrahydroisoquinoline derivative: PD, pharmacology
*tetrahydroisoquinoline derivative: CM, drug comparison
*estrogen: PD, pharmacology
*estrogen: CM, drug comparison
*cytochrome p450: EC, endogenous compound
tetrahydropapaveroline: PD, pharmacology
tetrahydropapaveroline: CM, drug comparison
estradiol: PD, pharmacology
estradiol: CM, drug comparison
2 hydroxyestradiol: PD, pharmacology
2 hydroxyestradiol: CM, drug comparison
coumestrol: PD, pharmacology
coumestrol: CM, drug comparison
genistein: PD, pharmacology
genistein: CM, drug comparison
salsolinol: PD, pharmacology
salsolinol: CM, drug comparison
salsoline: PD, pharmacology
salsoline: CM, drug comparison
salsolidine: PD, pharmacology
salsolidine: CM, drug comparison

L109 ANSWER 74 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
91268736 EMBASE Effects of inhibitors of protein tyrosine kinase activity and/or phosphatidylinositol turnover on differentiation of some human myelomonocytic leukemia cells. Makishima M.; Honma Y.; Hozumi M.; Sampi K.; Hattori M.; Umezawa K.; Motoyoshi K.. Department of Chemotherapy, Saitama Cancer Center Research Institute, Ina-machi, Saitama-362, Japan. LEUK. RES. 15/8 (701-708) 1991. ISSN: 0145-2126. CODEN: LEREDD. Pub. Country: United Kingdom. Language: English.

AB The activities of protein tyrosine kinase and phosphatidylinositol turnover have been found to be associated with cell growth and differentiation. We examined the effects of some inhibitors for these biochemical activities in human myelogenous leukemia cells. Genistein, which is known to inhibit the activities of protein tyrosine kinase, phosphatidylinositol turnover and topoisomerase II, induced nitroblue tetrazolium (NBT) reduction and lysozyme activity in ML-1, HL-60 and U937 cells. Morphological studies showed that genistein-induced differentiation of myeloblastic ML-1 cells into promyelocytes and of promyelocytic HL-60 cells into mature granulocytes. The differentiation-inducing effect of genistein was augmented by addition of 1.alpha., 25-dihydroxyvitamin D3 (VD3) or retinoic acid, VD3 being more effective than retinoic acid. Methyl 2,5-dihydroxycinamate, a protein tyrosine kinase inhibitor, had only a weak effect in inducing differentiation of ML-1 cells. On the other hand, psi-tectorigenin was more effective than genistein in inducing the differentiations of ML-1 and HL-60 cells. Psi-tectorigenin is reported to inhibit phosphatidylinositol turnover without inhibiting protein tyrosine kinase. Thus modulation of phosphatidylinositol turnover might be more important than that of protein tyrosine kinase activity for differentiation of some myelogenous leukemia cells.

CT EMTAGS: malignant neoplastic disease (0306); etiology (0135); blood and hemopoietic system (0927); mammal (0738); human (0888); human tissue, cells or cell components (0111); priority journal (0007); article (0060); enzyme (0990)
Medical Descriptors:
*cell differentiation
*myelomonocytic leukemia: ET, etiology
turnover time
cell growth
morphology

promyelocyte
granulocyte
human
human cell
priority journal
article
Drug Descriptors:
*protein tyrosine kinase: EC, endogenous compound
*protein tyrosine kinase: PD, pharmacology
*phosphatidylinositol: EC, endogenous compound
*phosphatidylinositol: PD, pharmacology
tectorigenin: EC, endogenous compound
tectorigenin: PD, pharmacology
genistein: PD, pharmacology
dna topoisomerase (atp hydrolysing): EC, endogenous compound
dna topoisomerase (atp hydrolysing): PD, pharmacology
nitroblue tetrazolium: EC, endogenous compound
nitroblue tetrazolium: PD, pharmacology
lysozyme: EC, endogenous compound
calcitriol: PD, pharmacology
retinoic acid: PD, pharmacology
herbimycin a: PD, pharmacology
unclassified drug
2,5 dihydroxycinnamic acid methyl ester: PD, pharmacology

L109 ANSWER 75 OF 79 MEDLINE
92192653 Serum lipid and lipoprotein fractions in bengal gram and biochanin A induced alterations in atherosclerosis. Gopalan R; Gracias D; Madhavan M. (Department of Pathology, Postgraduate Institute of Basic Medical Sciences, Madras..)INDIAN HEART JOURNAL, (1991 May-Jun) 43 (3) 185-9. Journal code: GHR. ISSN: 0019-4832. Pub. country: India. Language: English.
AB Serum lipids and lipoproteins were studied in rabbits fed on egg yolk supplemented diet to induce hypercholesterolemia. Bengal gram and synthetically pure isoflavone Biochanin A have been used as lipodiatic agents in this study. Rabbits were divided into four groups: Group A were fed on egg yolk supplement alone to form the positive control group, Group B were fed with 40 gms of overnight soaked bengal gram (Cicer arietinum), Group C were fed with 50 mgs of Biochanin A fortnightly, Group D was negative control group fed on pelleted laboratory feed. Serum samples were taken every month and total cholesterol, triglycerides and HDL cholesterol were estimated. The other lipoproteins like LDL cholesterol and VLDL cholesterol were obtained by calculations. The Group B and C showed a significant decrease of their lipids and lipoprotein in comparison to Group A thereby indicating the lipodiatic effect of these two substances. However, HDL cholesterol showed an increase in these two groups thereby proving that an increased HDL cholesterol has a protective effect on the atherosclerotic process.
CT Check Tags: Animal; Female; Male
Cholesterol: BL, blood
*Coronary Arteriosclerosis: BL, blood
*Isoflavones: PD, pharmacology
***Legumes**
*Lipids: BL, blood
Lipoproteins: BL, blood
Plant Extracts: PD, pharmacology
Rabbits
Triglycerides: BL, blood

L109 ANSWER 76 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
91198412 EMBASE Erbstatin and tyrphostins block protein-serine kinase activation and meiotic maturation of sea star oocytes. Daya-Makin M.; Pelech S.L.; Levitzki A.; Hudson A.T.. Biomedical Research Centre, University of British Columbia, Vancouver, B.C. V6T 123, Canada. BIOCHIM. BIOPHYS. ACTA MOL. CELL RES. 1093/1 (87-94) 1991. ISSN: 0167-4889. CODEN: BAMRDP. Pub. Country: Netherlands. Language: English.
AB The effects of ten putative protein-tyrosine kinase inhibitors on

the activation of protein-serine kinases and germinal vesicle breakdown (GVBD) in maturing sea star oocytes were investigated. Erbstatin and tyrphostins such as AG18 and AG125 blocked 1-methyladenine-induced GVBD in sea star oocytes with IC50 values of less than 20 .mu.M. Inhibition of the rate of GBVD was achieved even when these compounds were added up to 15 min after exposure of the oocytes to 1-methyladenine. The action of these substances on oocyte maturation was reversed by subsequent washing and culturing of the cells in natural sea water free of the inhibitors. Cell viability was maintained for at least 12 h in their presence, as assessed by Trypan blue dye exclusion. These inhibitors prevented the 1-methyladenine-induced activations of the histone H1 kinase p34(cdc2), the myelin basic protein kinase p44(mpk) and a ribosomal S6 peptide kinase. Erbstatin, AG18 and AG125 prevented 1-methyladenine-induced tyrosine dephosphorylation of p34(cdc2), and they inhibited tyrosine phosphorylation of p44(mpk). These studies imply that activation of a protein-tyrosine kinase may be necessary for stimulation of p34(cdc2) in maturing sea star oocytes.

CT EMTAGS: female genital system (0957); endocrine system (0970); nonhuman (0777); animal tissue, cells or cell components (0105); priority journal (0007); article (0060); enzyme (0990)
Medical Descriptors:
asterias
***oocyte maturation**
*meiosis
*germinal vesicle
nonhuman
animal cell
priority journal
article
Drug Descriptors:
*erbstatin: PD, pharmacology
ag 18: PD, pharmacology
ag 125: PD, pharmacology
ag 114: PD, pharmacology
compound 690c88: PD, pharmacology
ag 213: PD, pharmacology
ag 186: PD, pharmacology
compound 670c88: PD, pharmacology
ag 294: PD, pharmacology
unclassified drug
*1 methyladenine: PD, pharmacology
*histone h1: EC, endogenous compound
*myelin basic protein: EC, endogenous compound
*tyrphostin: PD, pharmacology
*protein kinase: EC, endogenous compound
genistein: PD, pharmacology

L109 ANSWER 77 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
89234689 EMBASE Isolation of isoflavonoids possessing antioxidant activity from the fermentation broth of Streptomyces sp.. Komiyama K.; Funayama S.; Anraku Y.; Mita A.; Takahashi Y.; Omura S.; Shimasaki H.. Kitasato Institute, Minato-ku, Tokyo 108, Japan. J. ANTIBIOT. 42/9 (1344-1349) 1989. ISSN: 0021-8820. CODEN: JANTAJ. Pub. Country: Japan. Language: English.

AB Three antioxidant isoflavonoids characterized as 4',7,8-trihydroxyisoflavone (1), 3',4',7-trihydroxyisoflavone (2) and 8-chloro-3',4',5,7-tetrahydroxyisoflavone (3) were isolated from the cultured broth of Streptomyces sp. OH-1049. Among them, 3 is a novel isoflavonoid possessing a chlorine atom in the molecule. In in vitro studies, these antibodies were found to possess antioxidant activity whereas showed almost no cytocidal activities against HeLa S3 cells.

CT EMTAGS: cell, tissue or organ culture (0103); bacterium (0762); fungus (0763); human tissue, cells or cell components (0111); human (0888); nonhuman (0777); **malignant neoplastic disease** (0306); infection (0310); chemical procedures (0107); priority journal (0007)
Medical Descriptors:

*drug isolation
*drug identification
*drug screening
*cytotoxicity
*antioxidant activity
cell culture
streptomyces
taxonomy
hela cell
Drug Descriptors:
daidzein
alpha tocopherol
8 chloro 3',4',5,7 tetrahydroxyisoflavone: AN, drug analysis
8 chloro 3',4',5,7 tetrahydroxyisoflavone: DV, drug development
4',6,7 trihydroxyisoflavone
4',7,8 trihydroxyisoflavone
3',4',7 trihydroxyisoflavone

L109 ANSWER 78 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
84210465 EMBASE Nonsteroidal estrogens of dietary origin: Possible roles in hormone-dependent disease. Setchell K.D.R.; Borriello S.P.; Hulme P.; et al.. Clinical Mass Spectrometry Section, Clinical Research Center, Harrow, Middlesex HA1 3UJ, United Kingdom. AM. J. CLIN. NUTR. 40/3 (569-578) 1984. CODEN: AJCNAC. Pub. Country: United States. Language: English.
AB Equol, a nonsteroidal estrogen of dietary origin, was recently identified in human urine, and is excreted in amounts comparable to the classical steroidal estrogens. We confirm here that phytoestrogens which are abundant in dietary soya protein are converted by human gastrointestinal flora to this weak estrogen. After the ingestion of meals containing cooked soya protein the urinary excretion of equol in four of six subjects studied increased by up to 1000-fold and this compound was the major phenolic compound found in the urine. These data also indicate that some subjects are unable to either produce or excrete equol despite the challenge of a diet containing soya. In view of the increasing use of commercial soya products in the diet and the capacity of human bacterial flora to synthesize this weak estrogen from the abundance of phytoestrogens in soya, the potential relevance of these observations to the disease implicating steroid hormones is discussed.
CT EMTAGS: therapy (0160); **malignant neoplastic disease** (0306); female genital system (0957); review (0001); human (0888); normal human (0800); endocrine system (0970); breast (0985)
Medical Descriptors:
*pharmacotherapy
***breast cancer**
***menstrual cycle**
***nutrition**
***soybean**
*phytoestrogen
*metabolism
*equol
*estradiol
*diethylstilbestrol
***daidzein**
***genistein**
***formononetin**
dysmenorrhea
breast carcinoma

L109 ANSWER 79 OF 79 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
78060757 EMBASE Morphological changes in the organs of ewes grazing oestrogenic subterranean clover. Adams N.R.. Div. Anim. Hlth, CSIRO, c/o Inst. Agric., Univ. West. Australia, Nedlands, Australia. RES.VET.SCI. 22/2 (216-221) 1977. CODEN: RVTSA. Language: English.
AB The morphological effects of phytoestrogen exposure were determined in 10 ewes exposed to subterranean clover for 60 days, compared with 10 controls. In a second experiment, the time course of the

development of the changes was studied. Typically estrogenic changes were observed in ovary, oviduct, uterus, cervix, vagina and mammary glands. There was an early increase in cervical mucus, followed by a decrease. The .delta. basophils of the pituitary became degranulated, and hyperactive in appearance. The adrenal and thyroid glands increased in weight, and thyroid epithelium increased in height. There appeared to be a temporary increase in neurophysin storage in the hypothalamus, and shrunken, hyperchromatic neurones were observed in the hypothalamus of some affected ewes. All changes were observed within three wk of exposure.

CT EMTAGS: theoretical study (0110); intoxication (0302); histology (0330); sheep (0737)

Medical Descriptors:

*phytoestrogen
*ovary
*uterine tube
*uterus
*histopathology
*sheep
*uterine cervix
*vagina
*breast
*adrenal gland
*thyroid gland
*hypophysis
*estrogen therapy
***diet**
***formononetin**
***genistein**
*genistein 4' methyl ether